



Europäisches Patentamt
European Patent Office
Office européen des brevets



⑪ Publication number: **0 617 132 A2**

⑫

EUROPEAN PATENT APPLICATION

⑳ Application number: **94302196.4**

⑤① Int. Cl.⁵: **C12Q 1/70, C12Q 1/68**

㉔ Date of filing: **28.03.94**

③① Priority: **26.03.93 US 40745**

④③ Date of publication of application:
28.09.94 Bulletin 94/39

⑧④ Designated Contracting States:
AT BE CH DE DK ES FR GB IT LI NL SE

⑦① Applicant: **GEN-PROBE INCORPORATED**
9880 Campus Point Drive
San Diego California 92121-1514 (US)

⑦② Inventor: **McDonough, Sherrol H.**
5005 Maynard Street
San Diego, California 92122 (US)
Inventor: **Ryder, Thomas B.**
1863 Angeles Glen
Escondido, California 92029 (US)
Inventor: **Yang, Yeasing**
13569 Glendcliff Way
San Diego, California 92130 (US)

⑦④ Representative: **Goldin, Douglas Michael**
J.A. KEMP & CO.
14, South Square
Gray's Inn
London WC1R 5LX (GB)

⑤④ Probes and method to detect human Immunodeficiency virus type 1.

⑤⑦ Amplification oligonucleotides and hybridization assay probes are provided which distinguish Human Immunodeficiency Virus type 1 from other viruses found in human blood tissues.
The probes are nucleotide polymers which hybridize to the nucleic acid region of Human Immunodeficiency Virus type 1 corresponding to bases 763-793 of HIV type 1, (HXB2 isolate GenBank accession number KO3455), or any of the regions corresponding to bases 1271-1301, 1358-1387, 1464-1489, 1501-1540, 1813-1845, 2969-2999, 3125-3161, 4148-4170, 4804-4832, 5950-5978, 9496-9523, 510-542 and 624-651.

This invention relates to the design and construction of amplification oligonucleotides and probes to Human Immunodeficiency Virus Type 1 (HIV), which allow detection of the organism in a test sample.

Laboratory diagnosis of Human Immunodeficiency Virus Type 1 in humans is currently performed by demonstration of the presence of viral antigen (p24) or anti-HIV-1 antibodies in serum. Direct detection of viral DNA, however, is a more useful diagnostic tool in some populations, such as infants born to seropositive mothers. Detection of viral DNA is more rapid and less hazardous than culture. Direct hybridization lacks adequate sensitivity in most patients (Shaw et al., *Science* 226: 1165-1171, 1984). Many references mention oligonucleotides said to have use in detection of Human Immunodeficiency Virus. Most of these references also mention the use of polymerase chain reaction (PCR). These references include the following: Kwok et al., *J. Virol.* 61: 1690-1694, 1987; Agius et al., *J. Virol. Meth.*, 30: 141-150, 1990; Albert and Fenyo, *J. Clin. Microbiol.* 28:1560-1564, 1990; Bell and Ratner, *AIDS Res. and Human Retroviruses* 5:87-95, 1989; Bruisten et al., *Vox Sang* 61:24-29, 1991; Clarke et al., *AIDS* 4:1133-1136, 1990; Coutlee et al., *Anal. Biochem.* 181:96-105, 1989; Dahlen et al., *J. Clin. Microbiol.* 29:798-804, 1991; Dudding et al., *Biochem. Biophys. Res. Comm.* 167:244-250, 1990; Ferrer-Le-Coeur et al., *Thrombosis and Haemostasis* 65:478-482, 1991; Goswami et al., *AIDS* 5:797-803, 1991; Grankvist et al., *AIDS* 5:575-578, 1991; Guatelli et al., *J. Virol.* 64:4093-4098, 1990; Hart et al., *Lancet* 2 (8611):596-599, 1988; Holland et al., *Proc. Natl. Acad. Sci. USA*, 88:7276-7280, 1991; Keller et al., *Anal. Biochem.* 177:27-32, 1989; Kumar et al., *AIDS Res. and Human Retroviruses* 5:345-354, 1989; Linz et al., *J. Clin. Chem. Clin. Biochem.* 28:5-13, 1990; Mano and Chermann, *Res. Virol.* 142:95-104, 1991; Mariotti et al., *AIDS* 4:633-637, 1990; Mariotti et al., *Transfusion* 30:704-706, 1990; Meyerhans et al., *Cell* 58:901-910, 1989; Mousset et al., *AIDS* 4:1225-1230, 1990; Ou et al., *Science* 239:295-297, 1988; Pang et al., *Nature* 343:85-89, 1990; Paterlini et al., *J. Med. Virol.* 30:53-57, 1990; Perrin et al., *Blood* 76:641-645, 1990; Preston et al., *J. Virol. Meth.* 33:383-390, 1991; Pritchard and Stefano, *Ann. Biol. Clin.* 48:492-497, 1990; Rudin et al., *Eur. J. Clin. Microbiol. Infect. Dis.* 10:146-156, 1991; Shoebridge et al., *AIDS* 5:221-224, 1991; Stevenson et al., *J. Virol.* 64:3792-3803, 1990; Truckenmiller et al., *Res. Immunol.* 140:527-544, 1989; Van de Perre, et al., *New Eng. J. Med.* 325:593-598, 1991; Varas et al., *BioTechniques* 11:384-391, 1991; Velpandi et al., *J. Virol.* 65:4847-4852, 1991; Williams et al., *AIDS* 4:393-398, 1990; Zachar et al., *J. Virol. Meth.* 33:391-395, 1991; Zack et al., *Cell* 61:213-222, 1990; Findlay et al., entitled "Nucleic acid test article and its use to detect a pre-determined nucleic acid," PCT/US90/00452; Gingeras et al., entitled "Nucleic acid probe assay methods and compositions," PCT/US87/01966; Brakel and Spadoro, entitled "Amplification capture assay," EPO application number 90124738.7, publication number 0 435 150 A2; Moncany and Montagnier, entitled "Séquences nucléotidiques issues du génome des retrovirus du typ hiv-1, hiv-2 et siv, et leurs applications notamment pour l'amplification des génomes de ces retrovirus et pour le diagnostic in-vitro des infections dues a ces virus," EPO application number 90401520.3, publication number 0 403 333 A2; Urdea, entitled "DNA-dependent RNA polymerase transcripts as reporter molecules for signal amplification in nucleic acid hybridization assays," PCT/US91/00213; Musso et al., entitled "Lanthanide chelate-tagged nucleic acid probes," PCT/US88/03735; Chang, entitled "Cloning and expression of HTLV-III DNA," EPO application number 85307260.1, publication number 0 185 444 A2; and Levenson, entitled "Diagnostic kit and method using a solid phase capture means for detecting nucleic acids," EPO application number 89311862.0, publication number 0 370 694; and Sninsky et al., U.S. Patent No. 5,008,182.

Summary of the Invention

This invention discloses novel amplification oligonucleotides and detection probes for the detection of Human Immunodeficiency Virus Type 1. The probes are capable of distinguishing between the Human Immunodeficiency Virus type 1 and its known closest phylogenetic neighbors. The amplification oligonucleotides and probes may be used in an assay for the detection and/or quantitation of Human Immunodeficiency Virus nucleic acid.

It is known that a nucleic acid sequence able to hybridize to a nucleic acid sequence sought to be detected ("target sequence") can serve as a probe for the target sequence. The probe may be labelled with a detectable moiety such as a radioisotope, antigen or chemiluminescent moiety to facilitate detection of the target sequence. A background description of the use of nucleic acid hybridization as a procedure for the detection of particular nucleic acid sequences is provided in Kohne, U.S. Patent No. 4,851,330, and Hogan et al., EPO Patent Application No. PCT/US87/03009, entitled "Nucleic Acid Probes for Detection and/or Quantitation of Non-Viral Organisms."

It is also known that hybridization may occur between complementary nucleic acid strands including: DNA/DNA, DNA/RNA, and RNA/RNA. Two single strands of deoxyribo- ("DNA") or ribo- ("RNA") nucleic acid, formed from nucleotides (including the bases adenine (A), cytosine (C), thymidine (T), guanine (G), uracil (U), or inosine (I)), may hybridize to form a double-stranded structure in which the two strands are held together

by hydrogen bonds between pairs of complementary bases. Generally, A is hydrogen bonded to T or U, while G is hydrogen bonded to C. At any point along the hybridized strands, therefore, one may find the classical base pairs AT or AU, TA or UA, GC, or CG. Thus, when a first single strand of nucleic acid contains sufficient contiguous complementary bases to a second, and those two strands are brought together under conditions which will promote their hybridization, double-stranded nucleic acid will result. Under appropriate conditions, DNA/DNA, RNA/DNA, or RNA/RNA hybrids may be formed. The present invention includes the use of probes or primers containing nucleotides differing in the sugar moiety, or otherwise chemically modified, which are able to hydrogen bond along the lines described above.

Thus, in a first aspect, the invention features hybridization assay probes able to distinguish Human Immunodeficiency Virus type 1 from other viruses found in human blood or tissues, and amplification oligonucleotides able to selectively amplify Human Immunodeficiency Virus nucleic acid. Specifically, the probes are nucleotide polymers which hybridize to the nucleic acid region of Human Immunodeficiency Virus type 1 corresponding to bases 763-793 of HIV type 1, (HXB2 isolate GenBank accession number K03455), or any of the regions corresponding to bases 1271-1301, 1358-1387, 1464-1489, 1501-1540, 1813-1845, 2969-2999, 3125-3161, 4148-4170, 4804-4832, 5950-5978, 9496-9523, 510-542, and 624-651; preferably, the oligonucleotide comprises, consists essentially of, or consists of the sequence (reading 5' to 3')

(SEQ ID NO: 1) GACTAGCGGAGGCTAGAAGGAGAGAGATGGG

(SEQ ID NO: 2) GAAGGCTTTCAGCCCAGAAGTAATACCCATG

(SEQ ID NO: 3) ATTTGCATGGCTGCTTGATGTCCCCCACT

(SEQ ID NO: 4) CTTCCCCTGGTTCTCTCATCTGGCC

(SEQ ID NO: 5) GTCATCCATCCTATTTGTTCTGAGGGTACTAGTAG

(SEQ ID NO: 6) CTCCCTGACATGCTGTCATCATTTCTTCTAGTG

(SEQ ID NO: 7) GTGGAAGCACATTGTACTGATATCTAATCCC

(SEQ ID NO: 8) GCTCCTCTATTTTGTCTATGCTGCCCTATTTCTAA

(SEQ ID NO: 9) CCTTTGTGTGCTGGTACCCATGC

(SEQ ID NO: 10) CTACTATTCTTTCCCCTGCACTGTACCCC

(SEQ ID NO: 11) AAAGCCTTAGGCATCTCCTATGGCAGGAA

(SEQ ID NO: 12) GCAGCTGCTTATATGCAGGATCTGAGGG

(SEQ ID NO: 13) CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG

(SEQ ID NO: 14) ATCTCTAGCAGTGGCGCCCGAACAGGGA

or RNA equivalents thereto (SEQ. ID. Nos. 67-80), or oligonucleotides complementary thereto (SEQ. ID. Nos. 53-66), or RNA equivalents to the oligonucleotides complementary thereto (SEQ. ID. Nos. 81-94).

The oligonucleotides are used with or without a helper probe as described below. The use of helper probes (e.g., SEQ. ID. Nos. 15-18) and complementary oligonucleotides to the helper probes (e.g., SEQ. ID. Nos. 95-98) and RNA equivalents thereto (e.g., SEQ. ID. Nos. 132-140) enhances nucleic acid hybridization.

By "consists essentially of" is meant that the probe is provided as a purified nucleic acid which under stringent hybridizing conditions hybridizes with the target sequence and not with other related target sequences present in either other virus nucleic acids or human nucleic acids. Such a probe may be linked to other nucleic acids which do not affect such hybridization. Generally, it is preferred that the probe is between 15 to 100 (most preferably between 20 and 50) bases in size. It may, however, be provided in a vector.

In a related aspect, the invention features the formation of nucleic acid hybrids formed by the hybridization of the probes of this invention with target nucleic acid under stringent hybridization conditions. Stringent hybridization conditions involve the use 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C. The hybrids are useful because they allow the specific detection of viral nucleic acid.

In another related aspect, the invention features amplification oligonucleotides useful for specific detection of Human Immunodeficiency Virus type 1 in an amplification assay. The amplification oligonucleotides are complementary to conserved regions of HIV genomic nucleic acid and are nucleotide polymers able to hybridize to regions of the nucleic acid of HIV corresponding to HIV-1 HXB2R bases 682-705, 800-822, 1307-1337, 1306-1330, 1315-1340, 1395-1425, 1510-1535, 1549-1572, 1743-1771, 1972-1989, 2868-2889, 3008-

3042, 3092-3124, 3209-3235, 4052-4079, 4176-4209, 4169-4206, 4394-4428, 4756-4778, 4835-4857, 4952-4969, 5834-5860, 5979-5999, 9431-9457, 9529-9555, 449-473, 550-577, 578-601, 579-600, 624-646, and 680-703.

Specifically, such amplification oligonucleotides consist, comprise, or consist essentially of those selected from (reading 5' to 3'):

- (X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),
 (X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),
 (X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),
 (X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),
 (X) CAGAAGGAGCCACCCCAAGATTTA (SEQ. ID. NO. 23),
 (X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),
 (X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),
 (X) AGTGACATAGCAGGAATA (SEQ. ID. NO. 26),
 (X) CCATCCTATTTGTTCTGAAGGGTAC (SEQ. ID. NO. 27),
 (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),
 (X) GAAACCTTGTTGAGTCCAAATGCGAACCC (SEQ. ID. NO. 29),
 (X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
 (X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
 (X) GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
 (X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),
 (X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
 (X) GCATTAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35),
 (X) GCACTGACTAATTTATCTACTTGTTTCATTTCTC (SEQ. ID. NO. 36),
 (X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37),
 (X) TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
 (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
 (X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
 (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),
 (X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
 (X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
 (X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),
 (X) GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45),
 (X) GTA CTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
 (X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
 (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
 (X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
 (X) GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
 (X) GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51)

and the RNA equivalents thereto (SEQ. ID. Nos. 99-131). Where (X) is nothing or a 5' oligonucleotide sequence that is recognized by an enzyme, including but not limited to the promoter sequence for T7, T3, or SP6 RNA polymerase, which enhances initiation or elongation of RNA transcription by an RNA polymerase. One example of X includes the sequence SEQ. ID. NO. 52: 5'-AATTTAATACGACTCACTATAGGGAGA-3'.

These amplification oligonucleotides are used in a nucleic acid amplification assay such as the polymerase chain reaction or an amplification reaction using RNA polymerase, DNA polymerase and RNase H or its equivalent, as described by Kacian and Fultz, *supra*, and by Sninsky et al. US. Patent No. 5,079,351, both hereby incorporated by reference herein.

The amplification oligonucleotides and probes of this invention offer a rapid, non-subjective method of identification and quantitation of a sample for specific sequences unique to strains of Human Immunodeficiency Virus type 1.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

Description of the Preferred Embodiments

We have discovered particularly useful DNA probes complementary to particular nucleic acid sequences of Human Immunodeficiency Virus type 1. Furthermore, we have successfully used these probes in a specific assay for the detection of Human Immunodeficiency Virus type 1, distinguishing it from the known and presumably most closely related taxonomic or phylogenetic neighbors found in human blood or tissues.

We have also identified particularly useful amplification oligonucleotides which are complementary to the Human Immunodeficiency Virus type 1 nucleic acid, and have used these oligonucleotides, *e.g.*, as primers or promoter primer combinations (*i.e.*, a primer having a promoter sequence attached), to amplify the nucleic acid of Human Immunodeficiency Virus, allowing its direct detection in a sample.

Useful guidelines for designing amplification oligonucleotides and probes with desired characteristics are described herein. The optimal sites for amplifying and probing contain two, and preferably three, conserved regions greater than about 15 bases in length, within about 350 bases, and preferably within 150 bases, of contiguous sequence. The degree of amplification observed with a set of primers or promoter/primers depends on several factors, including the ability of the oligonucleotides to hybridize to their complementary sequences and their ability to be extended enzymatically. Because the extent and specificity of hybridization reactions are affected by a number of factors, manipulation of those factors will determine the exact sensitivity and specificity of a particular oligonucleotide, whether perfectly complementary to its target or not. The importance and effect of various assay conditions are known to those skilled in the art as described in Hogan et al., EPO Patent Application No. PCT/US87/03009, entitled "Nucleic Acid Probes for Detection and/or Quantitation of Non-Viral Organisms"; and Milliman, entitled "Nucleic Acid Probes to *Haemophilus influenzae*," U.S. Serial No. 07/690,788, filed 4/25/91 assigned to the same assignee as the present application and hereby incorporated by reference herein.

The length of the target nucleic acid sequence and, accordingly, the length of the probe sequence can be important. In some cases, there may be several sequences from a particular region, varying in location and length, which will yield probes with the desired hybridization characteristics. In other cases, one sequence may be significantly better than another which differs merely by a single base. While it is possible for nucleic acids that are not perfectly complementary to hybridize, the longest stretch of perfectly homologous base sequence will normally primarily determine hybrid stability. While oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 10 to 50 bases in length and are sufficiently homologous to the target nucleic acid to hybridize under stringent hybridization conditions. We have found that optimal primers have target-binding regions of 18-38 bases, with a predicted T_m (melting temperature) to target of about 65°C.

Amplification oligonucleotides or probes should be positioned so as to minimize the stability of the oligomer:non-target (*i.e.*, nucleic acid with similar sequence to target nucleic acid) nucleic acid hybrid. It is preferred that the amplification oligomers and detection probes are able to distinguish between target and non-target sequences. In designing probes, the differences in these T_m values should be as large as possible (*e.g.*, at least 2°C and preferably 5°C).

Regions of the nucleic acid which are known to form strong internal structures inhibitory to hybridization are less preferred. Examples of such structures include hairpin loops. Likewise, probes with extensive self-complementarity should be avoided.

The degree of non-specific extension (primer-dimer or non-target copying) can also affect amplification efficiency, therefore primers are selected to have low self- or cross- complementarity, particularly at the 3' ends of the sequence. Long homopolymer tracts and high GC content are avoided to reduce spurious primer

extension. Commercial computer programs are available to aid in this aspect of the design. Available computer programs include MacDNASIS™ 2.0 (Hitachi Software Engineering American Ltd.) and OLIGO® ver. 4.1 (National Bioscience).

Hybridization is the association of two single strands of complementary nucleic acid to form a hydrogen bonded double strand. It is implicit that if one of the two strands is wholly or partially involved in a hybrid that it will be less able to participate in formation of a new hybrid. By designing a probe so that a substantial portion of the sequence of interest is single stranded, the rate and extent of hybridization may be greatly increased. If the target is an integrated genomic sequence then it will naturally occur in a double stranded form, as is the case with the product of the polymerase chain reaction (PCR). These double-stranded targets are naturally inhibitory to hybridization with a probe and require denaturation prior to the hybridization step. Finally, there can be intramolecular and intermolecular hybrids formed within a probe if there is sufficient self complementarity. Such structures can be avoided through careful probe design. Commercial computer programs are available to search for this type of interaction. Available computer programs include MacDNASIS™ 2.0 (Hitachi Software Engineering American Ltd.) and OLIGO® ver. 4.1 (National Bioscience).

Once synthesized, selected oligonucleotide probes may be labelled by any of several well known methods. 2 J. Sambrook, E.F. Fritsch and T. Maniatis, Molecular Cloning 11 (2d ed. 1989). Useful labels include radioisotopes as well as non-radioactive reporting groups. We currently prefer to use acridinium esters.

Oligonucleotide/target hybrid melting temperature may be determined by isotopic methods well known to those skilled in the art. It should be noted that the T_m for a given hybrid will vary depending on the hybridization solution being used. Sambrook, et al. supra.

Rate of hybridization may be measured by determining the $C_0t_{1/2}$. The rate at which a probe hybridizes to its target is a measure of the thermal stability of the target secondary structure in the probe region. The standard measurement of hybridization rate is the $C_0t_{1/2}$ which is measured as moles of nucleotide per liter times seconds. Thus, it is the concentration of probe times the time at which 50% of maximal hybridization occurs at that concentration. This value is determined by hybridizing various amounts of probe to a constant amount of target for a fixed time. The $C_0t_{1/2}$ is found graphically by standard procedure.

The following examples set forth oligonucleotide probes complementary to a unique nucleic acid sequence from a target organism, and their use in a hybridization assay.

Examples:

Probes specific for Human Immunodeficiency Virus type 1 were identified by comparison of sequences obtained from the published database GenBank. Sequences ID Nos. 1-12 were characterized and shown to be specific for Human Immunodeficiency Virus type 1. Phylogenetically near neighbors including Human Immunodeficiency Virus type 2, Human T-cell Leukemia Virus type 1 and Human T-Cell Leukemia Virus type 2 were used as comparisons with the sequence of Human Immunodeficiency Virus type 1.

Example 1. Probes for HIV

A hybridization protection assay was used to demonstrate the reactivity and specificity of the probes for Human Immunodeficiency Virus type 1. The probes were first synthesized with a non-nucleotide linker, then labelled with a chemiluminescent acridinium ester (AE) as described by Arnold, et al., PCT/US88/03361, entitled "Acridinium Ester Labeling and Purification of Nucleotide Probes," hereby incorporated by reference herein. The acridinium ester attached to an unhybridized probe is susceptible to hydrolysis and rendered non-chemiluminescent under mild alkaline conditions. However, the acridinium ester attached to hybridized probe is relatively resistant to hydrolysis. Thus, it is possible to assay for hybridization of acridinium ester-labelled probe by incubation with an alkaline buffer, followed by detection of chemiluminescence in a luminometer. Results are given in Relative Light Units (RLU); the quantity of photons emitted by the labelled-probe measured by the luminometer.

In the following experiment, DNA prepared from clones containing full or partial sequences of the target viruses was assayed. An example of a method for preparing the DNA from clones is provided by Sambrook et al, supra. The source of DNA for the clones was as follows; Human Immunodeficiency Virus type 1, BH10 (L. Ratner et al., Nature 312:277-284. 1985); Human Immunodeficiency Virus type 2 NIHZ (J.F. Zagury, et al., Proc. Natl. Acad. Sci. USA 85:5941-5945. 1988), Human T-cell leukemia virus type 1 pMT-2, (M. Clarke et al. Nature 305:60-62. 1983); Human T-cell leukemia virus type 2 (K. Shimotohmo et al. Proc. Natl. Acad. Sci. USA 82:3101-3105. 1985); and Human Hepatitis B Virus serotype ADW, obtained from ATCC(# 45020). Target in 50 μ l of 10 mM N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES), 10 mM ethylenediaminetetraacetic acid (EDTA), 1% lithium lauryl sulfate, pH 7.4, was denatured at 95°C for 5 min, cooled on wet ice, and 0.04 pmol of probe in 50 μ l of 0.1 M lithium succinate buffer, pH 4.7, 2% (w/v) lithium lauryl sulfate, 1.2 M lithium chloride, 10 mM EDTA and 20 mM ethyleneglycol-bis-(beta-aminoethyl ether) N,N,N',N'-tetraacetic acid

(EGTA) was added. Hybridization was carried out at 60°C for 10 min, followed by addition of 300 µl of 0.6 M sodium borate pH 8.5, 1% Triton X-100 and a second incubation at 60°C for 6 min to hydrolyze the AE on unhybridized probe. Samples were cooled in ice water for 1 min, placed at room temperature for another 3 min, and then analyzed in a LEADER 1 luminometer equipped with automatic injection of detection reagent I (containing 0.1% hydrogen peroxide and 1 mM nitric acid) and detection reagent II (containing 1 N sodium hydroxide and a surfactant component). Some of the hybridization reactions were enhanced with the addition of 4 pmol of unlabelled "helper probe" as disclosed in Hogan et al., U.S. Patent No. 5,030,557 entitled "Means and Methods for Enhancing Nucleic Acid Hybridization", hereby incorporated by reference herein. An RLU value greater than 5,000 RLU was a positive result; less than 5,000 RLU was a negative result.

The following data (Table 1) show that the probes do not cross react with viral DNA from closely related viruses found in human blood or tissues. The samples also gave a positive signal when tested with a probe specific to each target, thereby confirming sample adequacy.

Table 1. Hybridization Assay with HIV-1 probes.

Target:	1	2	3	4	5	6	7
Probe							
Sequence							
ID No:							
1	179,166	482	500	496	190	496	470
2	14,992	563	394	377	409	383	465
4	61,691	2,818	750	695	686	702	642
6	28,038	546	408	375	356	369	372
7	27,407	640	401	252	366	343	359
8	45,868	1,432	395	392	386	401	404
9	15,971	721	280	268	261	274	284
10	59,007	714	264	280	284	272	567
11	25,856	4,641	3,598	3,736	3,711	3,855	3,388
12	140,691	1,846	602	694	531	534	1,236

Target 1 = HIV-1 BH10 isolate 9 Kb SstI fragment, Target 2 = Human Immunodeficiency Virus Type 2 (NIH2 isolate) 9 Kb NaeI fragment, Target 3 = Human T-cell leukemia virus type 1 (pMT-2) 5' 4.6 Kb SstI-BamHI fragment; Target 4 = Human T-cell leukemia virus type 1 3' 4.4 Kb XbaI-SstI fragment,

Target 5 = Human T-cell leukemia virus type 2 3.5 Kb BamHI fragment, Target 6 = Human T-cell leukemia virus type 2 5 Kb BamHI fragment, Target 7 = Human Hepatitis B virus serotype ADW 1.3, 1.8 Kb BamHI fragments.

The above data confirm that the novel probes herein disclosed and claimed are capable of distinguishing Human Immunodeficiency Virus type 1 from these viruses found in human blood.

Example 2. Amplification of HIV by PCR

To demonstrate the reactivity of the primers and probes for Human Immunodeficiency Virus type 1, the following experiment was performed. Zero, 20, or 100 copies of plasmid DNA containing Human Immunode-

5 efficiency Virus DNA was linearized with a restriction endonuclease, and added to amplification reactions containing 50 pmol of each primer, 10 mM Tris HCl pH 8, 50 mM KCl, 1.25 mM MgCl₂, 0.25 mM each of dATP, dTTP, dCTP, dGTP, and 2.5 U Taq DNA polymerase in 50 µl. The reactions were incubated at 95°C for 1-2 min, and then cycled 35 times at 55°C for 15 sec, 72°C for 30 sec, and 95°C for 20 sec in a Perkin-Elmer 9600 thermocycler or 55°C for 30 sec, 72°C for 60 sec, and 95°C for 60 sec in a Perkin-Elmer 48 well thermocycler. Following cycling, the reactions were incubated at 72°C for 6-7 min and stored at 4°C. Ten µl of the product was analyzed by hybridization protection assay with 0.04 pmol of labeled probe. The data are shown in Table 2. RLU greater than 7,000 is considered a positive result.

10
15 Table 2. Amplification of Human Immunodeficiency Virus Type 1 by PCR

Primer Sequence ID Nos:	Probe Sequence ID. No.	Sample RLU		
		0 c	20 c	100 c
19/20*	1	886	827,202	723,008
21/22*	2	2,677	24,030	48,521
*23/25	3	370	144,082	603,456
25 *24/27	4	4,042	81,052	163,355
*26/28	5	263	273,023	593,022
*29/30	6	1,008	328,736	366,590
*31/32	7	3,394	73,690	86,168
30 *33/34	8	1,648	7,152	24,027
*35/36	9	560	82,980	145,681
*39/40	10	810	279,079	299,815
*39/41	10	886	362,914	427,500
35 42/43*	11	5,830	680,788	1,939,372
*44/45	12	1,387	21,428	130,709

The starred (*) primers had the sequence 5'-AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of the primer. 0 c = 0 copies of HIV DNA, 20 c = 20 copies of HIV DNA, 100 c = 100 copies of HIV DNA. Probe 1 was used in the presence of unlabeled helper probe SEQ. ID. No. 15. Probe 7 was used in the presence unlabeled helper probe SEQ. ID. No. 16. Probe 10 was used in the presence of unlabeled helper probe SEQ. ID. No. 17. Probe 12 was used in the presence of unlabeled helper probe SEQ. ID. No. 18. As the copy number increased, RLU increased. Thus, the primers of the present invention were able to successfully amplify, by PCR, HIV type 1 target sequences which were detected using the probes of the present invention.

Example 3. Patient samples

In this example, patient samples containing lysate prepared from 200,000 Ficoll-Hypaque purified white blood cells from individuals known to be infected with HIV type 1 or an individual not infected with HIV type 1 (negative) were analyzed as described in Example 2. These cells were prepared as described in Ryder and Kacian, entitled "Preparation of nucleic acid from blood," U.S. Serial number 07/898,785, filed 6/12/92. The results are shown in Table 3.

Table 3. PCR Assay

	Sample	RLU			
	Primer	Probe	Patient 1	Patient 2	Negative
	Sequence	Sequence			
20	ID Nos:	ID. No.			
	19/20*	1	27,616	71,981	886
	21/22*	2	34,949	35,483	565
25	*23/25	3	45,230	93,529*	455
	*24/27	4	2,355	25,329	1,052
	*26/28	5	22,345	26,014	369
	*31/32	7	200,418	130,486	481
30	*33/34	8	43,993	40,389	705
	*39/40	10	36,310	50,838	976
	*39/41	10	55,582	98,504	993
35	42/43*	11	99,028	207,605	6,057
	*44/45	12	55,082	80,388	1,496

The starred (*) primers had the sequence 5'-

AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of

the primer. The primers of the present invention were able

to amplify by PCR HIV type 1 target sequences present in individuals infected with HIV. The amplified target sequences were detected by the probes of the present invention. Thus, individuals containing HIV type 1 and an individual not containing HIV type 1 were correctly identified.

Example 4. Non-PCR Amplification

To show that the amplification oligomers also work in a transcription based amplification assay, 0, 2,000, or 20,000 copies of plasmid DNA containing HIV type 1 was linearized using a restriction endonuclease, and heated to 95°C for two min and cooled to 37°C for 1 min. Following addition of 800 U of MMLV reverse transcriptase the reactions were incubated for 12 min at 37°C, heated to 95°C for two min, and cooled to 37°C for

one min. 800 U of MMLV reverse transcriptase and 400 U of T7 RNA polymerase were added and the reactions were incubated for 3 hr at 37°C. The final amplification conditions were 70 mM Tris HCl, pH 8, 35 mM KCl, 15 mM KOH neutralized N-acetyl-cysteine, 6 mM rGTP, 4 mM rCTP, 4 mM rATP, 4 mM rUTP, 1 mM each of dTTP, dATP, dCTP and dGTP, and 22 mM MgCl₂ in 100 µl. Ten µl of each reaction was mixed with 40 µl of water and assayed as described for Table 1 except that the hybridization buffer contained 20 mM aldrithiol. The results in RLU are shown in Table 4.

Table 4. Transcription-Based Amplification Assay

10

RLU

Primers Sequence ID Nos:	Probe Sequence ID. No.	0 c	2,000 c	20,000 c
19/20*	1	681	24,170	190,536
21/22*	2	793	62,476	523,770
*23/25	3	2,239	812,577	1,126,045
*24/27	4	1,901	160,274	780,351
*26/28	5	2,555	877,893	1,167,756
*29/30	6	868	299,255	880,119
*31/32	7	871	129,732	969,034
*33/34	8	710	134,887	986,266
*35/36	9	884	128,981	1,021,865
*39/40	10	1,597	375,629	478,883
*39/41	10	1,264	499,304	495,509
*44/45	12	2,426	41,684	542,339

The starred (*) primers had the sequence 5'-AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of the primer. Probe 1 was used in the presence of unlabelled helper probe SEQ. ID. No. 15. Probe 7 was used in the presence of unlabelled helper probe SEQ. ID. No. 16, probe 10 was used in the presence of unlabelled helper probe SEQ. ID. No. 17, and probe 12 was used in the presence of unlabelled helper probe SEQ. ID. No. 18. 0 c = 0 copies of HIV DNA, 2,000 c = 2,000 copies of HIV DNA, 20,000 c = 20,000 copies of HIV DNA.

50

As the copy number increased RLU also increased. Thus, the primers of the present invention can be used to amplify HIV type 1 target sequences using a transcription based amplification assay and the amplified target sequences can be detected using the probes of the present invention.

55 Example 5.

This example demonstrates the ability of probes for Human Immunodeficiency Virus type 1 to detect low-levels of target oligomer produced in a transcription based amplification assay. Zero or 10 copies of plasmid

DNA containing HIV type I sequence was linearized using a restriction endonuclease, heated in the presence of 1 µg of human DNA to 95°C for eight minutes, and then cooled to 42°C for six minutes. Amplification was carried out at 42°C for two hours using 800 U MMLV reverse transcriptase and 400 U of T7 RNA polymerase, in the following reaction mix: 50 mM Tris HCl pH 8, 17.5 mM MgCl₂, 0.05 mM zinc acetate, 10% glycerol, 6.25 mM rGTP, 2.5 mM rCTP, 6.25 mM rATP, 2.5 mM rUTP, 0.2 mM dTTP, 0.2 mM dATP, 0.2 mM, 0.2 mM dCTP and 0.2 mM dGTP. Primer SEQ ID NOS. 26, 28, and 41 were used at a concentration of 30 pmol, primer SEQ ID NO. 39 was used at a concentration of 15 pmol. The entire reaction was analyzed using the hybridization protection assay with 0.04 pmol of probe in 100 µl of the hybridization buffer (supplemented with 20 mM aldri-thiol) as described in Example 1. Probe SEQ ID NO. 10 was hybridized in the presence of 2 pmol unlabeled helper SEQ ID NO. 17.

Table 5. Low Level Transcription-Based Amplification Assay

Primers SEQ ID NOS.	Probe SEQ	RLU	
		0 copies	10 copies
*26/28	5	1,293	64,639
*39/40	10	2,143	564,185

The 10 copy values represent the average of ten replicates. The starred (*) primers had the sequence 5'-AATTTAATACGACTCACTATAGGGAGA-3' attached to the 5' end of the primer.

Other embodiments are within the following sequence listing.

(1) GENERAL INFORMATION:

5 (i) APPLICANT: Sherrol H. McDonough, Thomas B. Ryder,
Yeasing Yang

10 (ii) TITLE OF INVENTION: NUCLEIC ACID AMPLIFICATION
OLIGONUCLEOTIDES AND PROBES
TO HUMAN IMMUNODEFICIENCY VIRUS TYPE 1

(iii) NUMBER OF SEQUENCES: 140

15 (iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Lyon & Lyon
(B) STREET: 611 West Sixth Street
(C) CITY: Los Angeles
(D) STATE: California
20 (E) COUNTRY: USA
(F) ZIP: 90017

(v) COMPUTER READABLE FORM:

25 (A) MEDIUM TYPE: 3.5" Diskette, 1.44 Mb storage
(B) COMPUTER: IBM PS/2 Model 50Z or 55SX
(C) OPERATING SYSTEM: IBM P.C. DOS (Version 3.30)
(D) SOFTWARE: WordPerfect (Version 5.0)

(vi) CURRENT APPLICATION DATA:

30 (A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

35 (vii) PRIOR APPLICATION DATA:

Prior applications total,
including application
described below:

2

40 (A) APPLICATION NUMBER: U.S. Serial No. 07/550,837
(B) FILING DATE: 7/10/90
(A) APPLICATION NUMBER: U.S. Serial No. 07/379,501
45 (B) FILING DATE: 7/11/89

50

55

5 (viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Warburg, Richard J.
 (B) REGISTRATION NUMBER: 32,327
 (C) REFERENCE/DOCKET NUMBER: 196/189

10 (ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: (213) 489-1600
 (B) TELEFAX: (213) 955-0440
 (C) TELEX: 67-3510

15 (2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 1:

GACTAGCGGA GGCTAGAAGG AGAGAGATGG G 31

25 (3) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 2:

35 GAAGGCTTTC AGCCCAGAAG TAATACCCAT G 31

(4) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 3:

45 ATTTGCATGG CTGCTTGATG TCCCCCACT 30

50

55

(5) INFORMATION FOR SEQ ID NO: 4:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
10 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 4:

CTTCCCCTTG GTTCTCTCAT CTGGCC 26

15 (6) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37
20 (B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 5:

25 GTCATCCATC CTATTTGTTC CTGAAGGGTA CTAGTAG 37

(7) INFORMATION FOR SEQ ID NO: 6:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
35 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 6:

CTCCCTGACA TGCTGTCATC ATTTCTTCTA GTG 33

40 (8) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31
45 (B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 7:

50

55

GTGGAAGCAC ATTGTACTGA TATCTAATCC C 31

(9) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 8:

GCTCCTCTAT TTTTGGTCTA TGCTGCCCTA TTTCTAA 37

(10) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 9:

CCTTTGTGTG CTGGTACCCA TGC 23

(11) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 10:

CTACTATTCT TTCCCCTGCA CTGTACCCC 29

(12) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 11:

5 AAAGCCTTAG GCATCTCCTA TGGCAGGAA 29

(13) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 28
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

15 (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 12:

GCAGCTGCTT ATATGCAGGA TCTGAGGG 28

(14) INFORMATION FOR SEQ ID NO: 13:

20 (i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 33
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 13:

30 CAAGGCAAGC TTTATTGAGG CTTAAGCAGT GGG 33

(15) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 28
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

40 (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 14:

ATCTCTAGCA GTGGCGCCCG AACAGGGA 28

(16) INFORMATION FOR SEQ ID NO: 15:

45 (i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

55

(D) TOPOLOGY:

linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 15:

5

TGCGAGAGCG TCAGTATTAA GCGG 24

(17) INFORMATION FOR SEQ ID NO: 16:

10

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 36
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 16:

20

CTACTTTGGA ATATTGCTGG TGATCCTTTC CATCCC 36

(18) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 17:

30

CCAATCCCCC CTTTCTTTT AAAATTGTGG ATG 33

(19) INFORMATION FOR SEQ ID NO: 18:

35

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 24
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 18:

45

CTCGCCACTC CCCAGTCCCG CCCA 24

(20) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH: 24

55

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 19:

CTCGACGCAG GACTCGGCTT GCTG 24

10

(21) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 23
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 20:

20

CTCCCCCGCT TAATACTGAC GCT 23

(22) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 31
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 21:

GGCAAATGGT ACATCAGGCC ATATCACCTA G 31

35

(23) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 25
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 22:

45

GGGGTGGCTC CTTCTGATAA TGCTG 25

(24) INFORMATION FOR SEQ ID NO: 23:

50

(i) SEQUENCE CHARACTERISTICS:

55

(A) LENGTH: 26
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 23:

CAGAAGGAGC CACCCCACAA GATTTA 26

(25) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 24:

GACCATCAAT GAGGAAGCTG CAGAATG 27

(26) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 25:

CCCATTCTGC AGCTTCCTCA TTGAT 25

(27) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 26:

AGTGACATAG CAGGAACTA 19

(28) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 27:

10 CCATCCTATT TGTCCTGAA GGGTAC 26

(29) INFORMATION FOR SEQ ID NO: 28:

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 20 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 28:

AGATTTCTCC TACTGGGATA GGT 23

25 (30) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 30
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

35 (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 29:

GAAACCTTGT TGAGTCCAAA ATGCGAACCC 30

(31) INFORMATION FOR SEQ ID NO: 30:

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18
 (B) TYPE: nucleic acid
 45 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 30:

50

55

TGTGCCCTTC TTTGCCAC 18

(32) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	22
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 31:

CAGTACTGGA TGTGGGTGAT GC 22

(33) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	35
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 32:

GTCATGCTAC TTTGGAATAT TTCTGGTGAT CCTTT 35

(34) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	33
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 33:

CAATACATGG ATGATTTGTA TGTAGGATCT GAC 33

(35) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	28
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 34:

5 ACCAAAGGAA TGGAGGTTCT TTCTGATG 28

(36) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 35:

15 GCATTAGGAA TCATTCAAGC ACAACCAG 28

(37) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 34
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 36:

30 GCACTGACTA ATTTATCTAC TTGTTTCATTT CCTC 34

(38) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 38
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 37:

40 GGGATTGGAG GAAATGAACA AGTAGATAAA TTAGTCAG 38

(39) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 35
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

55

(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 38:

TGTGTACAAT CTAGTTGCCA TATTCCTGGA CTACA 35

(40) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 39:

CAAATGGCAG TATTCATCCA CA 22

(41) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 40:

GTTTGTATGT CTGTTGCTAT TAT 23

(42) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 41:

CCCTTCACCT TTCCAGAG 18

(43) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 42:

GAGCCCTGGA AGCATCCAGG AAGTCAG 27

(44) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 21
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 43:

CTTCGTCGCT GTCTCCGCTT C 21

(45) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 44:

CAAGGGACTT TCCGCTGGGG ACTTTCC 27

(46) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 45:

GTCTAACCAG AGAGACCCAG TACAGGC 27

(47) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 46:

GTACTGGGTC TCTCTGGTTA GACCA 25

(48) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 47:

CACACAACAG ACGGGCACAC ACTACTTG 28

(49) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 48:

CTGAGGGATC TCTAGTTACC AGAGT 25

(50) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 49:

CTCTGGTAAC TAGAGATCCC TCA 23

(51) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 50:

10 GTTCGGGCGC CACTGCTAGA GAT 23

(52) INFORMATION FOR SEQ ID NO: 51:

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 20 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 51:

GCAAGCCGAGT CCTGCGTCG AGA 23

25 (53) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 27
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 52:

35 AATTTAATAC GACTCACTAT AGGGAGA 27

(54) INFORMATION FOR SEQ ID NO: 53:

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31
 (B) TYPE: nucleic acid
 45 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 53:

50

55

CCCATCTCTC TCCTTCTAGC CTCCGCTAGT C 31

(55) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 54:

CATGGGTATT ACTTCTGGGC TGAAAGCCTT C 31

(56) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	30
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 55:

AGTGGGGGGA CATCAAGCAG CCATGCAAAT 30

(57) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	26
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 56:

GGCCAGATGA GAGAACCAAG GGAAG 26

(58) INFORMATION FOR SEQ ID NO: 57:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	37
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 57:

CTACTAGTAC CCTTCAGGAA CAAATAGGAT GGATGAC

37

(59) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	33
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 58:

CACTAGAAGA AATGATGACA GCATGTCAGG GAG

33

(60) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 59:

GGGATTAGAT ATCAGTACAA TGTGCTTCCA C

31

(61) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	37
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 60:

TTAGAAATAG GGCAGCATAG AACAAAAATA GAGGAGC

37

(62) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	23
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single

(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 61:

5 GCATGGGTAC CAGCACACAA AGG 23

(63) INFORMATION FOR SEQ ID NO: 62:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 29
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

15 (ii) SEQUENCE DESCRIPTION : SEQ ID NO: 62:

GGGGTACAGT GCAGGGGAAA GAATAGTAG 29

20 (64) INFORMATION FOR SEQ ID NO: 63:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 29
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 63:

30 TTCCTGCCAT AGGAGATGCC TAAGGCTTT 29

(65) INFORMATION FOR SEQ ID NO: 64:

35 (i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 64:

45 CCCTCAGATC CTGCATATAA GCAGCTGC 28

(66) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:

50

55

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

5

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 65:

CCCACTGCTT AAGCCTCAAT AAAGCTTGCC TTG 33

10

(67) INFORMATION FOR SEQ ID NO: 66:

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

20

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 66:

TCCCTGTTCG GCGCCACTG CTAGAGAT 28

(68) INFORMATION FOR SEQ ID NO: 67:

25

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 31
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 67:

GACUAGCGGA GGCUAGAAGG AGAGAGAUGG G 31

35

(69) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 31
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

45

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 68:

GAAGGCUUUC AGCCCAGAAG UAAUACCCAU G 31

50

(70) INFORMATION FOR SEQ ID NO: 69:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 69:

AUUUGCAUGG CUGCUUGAUG UCCCCCACU 30

(71) INFORMATION FOR SEQ ID NO: 70:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 70:

CUUCCCCUUG GUUCUCUCAU CUGGCC 26

(72) INFORMATION FOR SEQ ID NO: 71:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 71:

GUCAUCCAUC CUAUUUGUUC CUGAAGGGUA CUAGUAG 37

(73) INFORMATION FOR SEQ ID NO: 72:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 72:

CUCCCUGACA UGCUGUCAUC AUUUCUUCUA GUG 33

(74) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 73:

GUGGAAGCAC AUUGUACUGA UAUCUAAUCC C 31

(75) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	37
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 74:

GCUCCUCUAU UUUUGUUCUA UGCUGCCCUA UUUCUAA 37

(76) INFORMATION FOR SEQ ID NO: 75:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	23
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 75:

CCUUUGUGUG CUGGUACCCA UGC 23

(77) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	29
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 76:

CUACUAUUCU UUCCCCUGCA CUGUACCCC 29

(78) INFORMATION FOR SEQ ID NO: 77:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	29
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 77:

AAAGCCUUG GCAUCUCCUA UGGCAGGAA 29

(79) INFORMATION FOR SEQ ID NO: 78:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	28
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 78:

GCAGCUGCUU AUAUGCAGGA UCUGAGGG 28

(80) INFORMATION FOR SEQ ID NO: 79:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	33
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 79:

CAAGGCAAGC UUUAUUGAGG CUUAAGCAGU GGG 33

(81) INFORMATION FOR SEQ ID NO: 80:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	28
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 80:

AUCUCUAGCA GUGGCGCCCG AACAGGGA 28

5

(82) INFORMATION FOR SEQ ID NO: 81:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 81:

15

CCCAUCUCUC UCCUUCUAGC CUCCGCUAGU C 31

(83) INFORMATION FOR SEQ ID NO: 82:

20

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 82:

30

CAUGGGUAUU ACUUCUGGGC UGAAAGCCUU C 31

(84) INFORMATION FOR SEQ ID NO: 83:

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 83:

40

AGUGGGGGGA CAUCAAGCAG CCAUGCAAA U 31

(85) INFORMATION FOR SEQ ID NO: 84:

45

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH:	26
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single

55

(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 84:

GGCCAGAUGA GAGAACCAAG GGGAAG 26

(86) INFORMATION FOR SEQ ID NO: 85:

(1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 85:

CUACUAGUAC CCUUCAGGAA CAAAUAGGAU GGAUGAC 37

(87) INFORMATION FOR SEQ ID NO: 86:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 86:

CACUAGAAGA AAUGAUGACA GCAUGUCAGG GAG 33

(88) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 87:

GGGAUUAGAU AUCAGUACAA UGUGCUUCCA C 31

(89) INFORMATION FOR SEQ ID NO: 88:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

5

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 88:

UUAGAAAUAG GGCAGCAUAG AACAAAAUA GAGGAGC 37

10

(90) INFORMATION FOR SEQ ID NO: 89:

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 23
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 89:

20

GCAUGGGUAC CAGCACACAA AGG 23

(91) INFORMATION FOR SEQ ID NO: 90:

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 29
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

30

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 90:

GGGGUACAGU GCAGGGGAAA GAAUAGUAG 29

35

(92) INFORMATION FOR SEQ ID NO: 91:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 29
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 91:

45

UUCCUGCCAU AGGAGAUGCC UAAGGCUUU 29

(93) INFORMATION FOR SEQ ID NO: 92:

50

55

(1) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 92:

CCCUCAGAUC CUGCAUAUAA GCAGCUGC 28

(94) INFORMATION FOR SEQ ID NO: 93:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 93:

CCCACUGCUU AAGCCUCAAU AAAGCUUGCC UUG 33

(95) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 94:

UCCCUGUUCG GCGCCACUG CUAGAGAU 38

(96) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 95:

CCGCTTAATA CTGACGCTCT CGCA 24

(97) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 36
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 96:

GGGATGGAAA GGATCACCAG CAATATTCCA AAGTAG 36

(98) INFORMATION FOR SEQ ID NO: 97:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 97:

CATCCACAAT TTAAAAGAA AAGGGGGGAT TGG 33

(99) INFORMATION FOR SEQ ID NO: 98:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 98:

TGGGCGGGAC TGGGGAGTGG CGAG 24

(100) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 99:

00280Y
 CUCGACGCAG GACUCGGCUU GCUG

24

(101) INFORMATION FOR SEQ ID NO: 100:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	23
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 100:

CUCCCCCGCU UAAUACUGAC GCU 23

(102) INFORMATION FOR SEQ ID NO: 101:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	31
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 101:

GGCAAAUGGU ACAUCAGGCC AUAUCACCUA G 31

(103) INFORMATION FOR SEQ ID NO: 102:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	25
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 102:

GGGGUGGCUC CUUCUGAUAA UGCUG 25

(104) INFORMATION FOR SEQ ID NO: 103:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	26
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 103:

CAGAAGGAGC CACCCCACAA GAUUUA 26

5

(105) INFORMATION FOR SEQ ID NO: 104:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH:	27
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

15

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 104:

GACCAUCAAU GAGGAAGCUG CAGAAUG 27

(106) INFORMATION FOR SEQ ID NO: 105:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	25
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

25

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 105:

CCCAUUCUGC AGCUUCCUCA UUGAU 25

30

(107) INFORMATION FOR SEQ ID NO: 106:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	19
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

35

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 106:

AGUGACAUAG CAGGAACUA 19

40

(108) INFORMATION FOR SEQ ID NO: 107:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	26
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single

50

55

(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 107:

5 CCAUCCUAUU UGUUCCUGAA GGGUAC 26

(109) INFORMATION FOR SEQ ID NO: 108:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 108:

15 AGAUUUCUCC UACUGGGAUA GGU 23

20 (110) INFORMATION FOR SEQ ID NO: 109:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 30
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 109:

30 GAAACCUUGU UGAGUCCAAA AUGCGAACCC 30

(111) INFORMATION FOR SEQ ID NO: 110:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 18
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 110:

40 UGUGCCCUUC UUUGCCAC 18

45 (112) INFORMATION FOR SEQ ID NO: 111:

(i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 22

(B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

5

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 111:

CAGUACUGGA UGUGGGUGAU GC 22

10

(113) INFORMATION FOR SEQ ID NO: 112:

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 35
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 112:

20

GUCAUGCAC UUGGAAUUAU UUCUGGUGAU CCUUU 35

(114) INFORMATION FOR SEQ ID NO: 113:

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

30

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 113:

CAAUACAUGG AUGAUUUGUA UGUAGGAUCU GAC 33

35

(115) INFORMATION FOR SEQ ID NO: 114:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 114:

45

ACCAAAGGAA UGGAGGUUCU UUCUGAUG 28

(116) INFORMATION FOR SEQ ID NO: 115:

50

(i) SEQUENCE CHARACTERISTICS:

55

(A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 115:

GCAUUAGGAA UCAUUCAAGC ACAACCAG 28

(117) INFORMATION FOR SEQ ID NO: 116:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 116:

GCACUGACUA AUUUAUCUAC UUGUUCAUUU CCUC 34

(118) INFORMATION FOR SEQ ID NO: 117:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 117:

GGGAUUGGAG GAAUGAACA AGUAGAUAAA UUAGUCAG 38

(119) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 35
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 118:

UGUGUACAAU CUAGUUGCCA UAUUCCUGGA CUACA 35

(120) INFORMATION FOR SEQ ID NO: 119:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 119:

CAAAUGGCAG UAUUCAUCCA CA 22

(121) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 120:

GUUUGUAUGU CUGUUGCUAU UAU 23

(122) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 121:

CCCUUCACCU UCCAGAG 18

(123) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 122:

GAGCCUGGA AGCAUCCAGG AAGUCAG 27

(124) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	21
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 123:

CUUCGUCGCU GUCUCCGCUU C 21

(125) INFORMATION FOR SEQ ID NO: 124:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	27
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 124:

CAAGGGACUU UCCGCUGGGG ACUUUCC 27

(126) INFORMATION FOR SEQ ID NO: 125:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	27
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 125:

GUCUAACCAG AGAGACCCAG UACAGGC 27

(127) INFORMATION FOR SEQ ID NO: 126:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:	25
(B) TYPE:	nucleic acid
(C) STRANDEDNESS:	single
(D) TOPOLOGY:	linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 126:

GUACUGGGUC UCUCUGGUUA GACCA 25

(128) INFORMATION FOR SEQ ID NO: 127:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 127:

CACACAACAG ACGGGCACAC ACUACUUG 28

(129) INFORMATION FOR SEQ ID NO: 128:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 128:

CUGAGGGAUC UCUAGUUACC AGAGU 25

(130) INFORMATION FOR SEQ ID NO: 129:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 129:

CUCUGGUAAC UAGAGAUCCC UCA 23

(131) INFORMATION FOR SEQ ID NO: 130:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 130:

GUUCGGGCGC CACUGCUAGA GAU 23

(132) INFORMATION FOR SEQ ID NO: 131:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 131:

GCAAGCCGAG UCCUGCGUCG AGA 23

(133) INFORMATION FOR SEQ ID NO: 132:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 132:

UGCGAGAGCG UCAGUAUUA GCGG 24

(134) INFORMATION FOR SEQ ID NO: 133:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 36
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 133:

CUACUUUGGA AUAUUGCUGG UGAUCCUUUC CAUCCC 36

(135) INFORMATION FOR SEQ ID NO: 134:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 134:

CCAAUCCCCC CUUUUCUUUU AAAAUUGUGG AUG 33

(136) INFORMATION FOR SEQ ID NO: 135:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 135:

CUCGCCACUC CCCAGUCCCG CCCA 24

(137) INFORMATION FOR SEQ ID NO: 136:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 136:

CCGCUUAAUA CUGACGCUCU CGCA 24

(138) INFORMATION FOR SEQ ID NO: 137:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 36
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 137:

GGGAUGGAAA GGAUCACCAG CAAUAUCCA AAGUAG 36

(139) INFORMATION FOR SEQ ID NO: 138:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 138:

CAUCCACAAU UUUAAAAGAA AAGGGGGGAU UGG 33

(140) INFORMATION FOR SEQ ID NO: 139:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) SEQUENCE DESCRIPTION : SEQ ID NO: 139:

UGGGCGGGAC UGGGAGUGG CGAG 24

Claims

1. An oligonucleotide consisting essentially of a sequence selected from the group of:

(SEQ ID NO: 1) GACTAGCGGAGGCTAGAAGGAGAGAGATGGG,
(SEQ ID NO: 2) GAAGGCTTTCAGCCCAGAAGTAATACCCATG,
(SEQ ID NO: 3) ATTTGCATGGCTGCTTGATGTCCCCCCT,
(SEQ ID NO: 4) CTTCCCCTTGGTTCTCTCATCTGGCC,
(SEQ ID NO: 5) GTCATCCATCCTATTTGTTCTGAAGGGTACTAGTAG,
(SEQ ID NO: 6) CTCCCTGACATGCTGTCATCATTCTCTTAGTG,
(SEQ ID NO: 7) GTGGAAGCACATTGTACTGATATCTAATCCC,
(SEQ ID NO: 8) GCTCCTCTATTTTTGTTCTATGCTGCCCTATTTCTAA,
(SEQ ID NO: 9) CCTTTGTGTGCTGGTACCCATGC,
(SEQ ID NO: 10) CTACTATTCTTTCCCCTGCACTGTACCCC,
(SEQ ID NO: 11) AAAGCCTTAGGCATCTCCTATGGCAGGAA,
(SEQ ID NO: 12) GCAGCTGCTTATATGCAGGATCTGAGGG,
(SEQ ID NO: 13) CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG,
(SEQ ID NO: 14) ATCTCTAGCAGTGGCGCCCGAACAGGGA,
(SEQ ID NO: 53) CCCATCTCTCTCCTTCTAGCCTCCGCTAGTC,
(SEQ ID NO: 54) CATGGGTATTACTTCTGGGCTGAAAGCCTTC,
(SEQ ID NO: 55) AGTGGGGGACATCAAGCAGCCATGCAAAT,
(SEQ ID NO: 56) GGCCAGATGAGAGAACCAAGGGGAG,
(SEQ ID NO: 57) CTACTAGTACCCTTCAGGAACAAATAGGATGGATGAC,
(SEQ ID NO: 58) CACTAGAAGAAATGATGACAGCATGTCAGGGAG,
(SEQ ID NO: 59) GGGATTAGATATCAGTACAATGTGCTTCCAC,
(SEQ ID NO: 60) TTAGAAATAGGGCAGCATAGAACAAAAATAGAGGAGC,
(SEQ ID NO: 61) GCATGGGTACCAGCACACAAAGG,
(SEQ ID NO: 62) GGGGTACAGTGCAGGGGAAAGAATAGTAG,
(SEQ ID NO: 63) TTCCTGCCATAGGAGATGCCTAAGGCTTT,
(SEQ ID NO: 64) CCCTCAGATCCTGCATATAAGCAGCTGC,
(SEQ ID NO: 65) CCCACTGCTTAAGCCTCAATAAAGCTTGCTTG,
(SEQ ID NO: 66) TCCCTGTTCCGGGCGCCACTGCTAGAGAT,
(SEQ ID NO: 67) GACUAGCGGAGGCUAGAAGGAGAGAGAUGGG,

(SEQ ID NO:68) GAAGGCUUUCAGCCCAGAAGUAAUACCCAUG,
 (SEQ ID NO:69) AUUUGCAUGGCUGCUUGAUGUCCCCCACU,
 (SEQ ID NO:70) CUUCCCCUUGGUUCUCUCAUCUGGCC,
 5 (SEQ ID NO:71) GUCAUCCAUCCUAUUUGUCCUGAAGGGUACUAGUAG,
 (SEQ ID NO:72) CUCCCUGACAUGCUGUCAUUAUUUCUUCUAGUG,
 (SEQ ID NO:73) GUGGAAGCACAUUGUACUGAUUAUCUAAUCCC,
 10 (SEQ ID NO:74) GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA,
 (SEQ ID NO:75) CCUUUGUGUGCUGGUACCCAUGC,
 (SEQ ID NO:76) CUACUAUUCUUUCCCCUGCACUGUACCCC,
 (SEQ ID NO:77) AAAGCCUUAGGCAUCUCCUAUGGCAGGAA,
 15 (SEQ ID NO:78) GCAGCUGCUUAUAUGCAGGAUCUGAGGG,
 (SEQ ID NO:79) CAAGGCAAGCUUUAUUGAGGCUUAAGCAGUGGG,
 (SEQ ID NO:80) AUCUCUAGCAGUGGCGCCCGAACAGGGA,
 20 (SEQ ID NO:81) CCCAUCUCUCUCCUUCUAGCCUCCGCUAGUC,
 (SEQ ID NO:82) CAUGGGUAUUACUUCUGGGCUGAAAGCCUUC,
 (SEQ ID NO:83) AGUGGGGGGACAUCAAGCAGCCAUGCAAAU,
 (SEQ ID NO:84) GGCCAGAUGAGAGAACCAAGGGGAAG,
 25 (SEQ ID NO:85) CUACUAGUACCCUUCAGGAACAAAUAGGAUGGAUGAC,
 (SEQ ID NO:86) CACUAGAAGAAAUGAUGACAGCAUGUCAGGGAG,
 (SEQ ID NO:87) GGGAUUAGAUUAUCAGUACAAUGUGCUUCCAC,
 30 (SEQ ID NO:88) UUAGAAAUAGGGCAGCAUAGAACAAAAUAGAGGAGO,
 (SEQ ID NO:89) GCAUGGGUACCAGCACACAAAGG,
 (SEQ ID NO:90) GGGGUACAGUGCAGGGGAAAGAAUAGUAG,
 35 (SEQ ID NO:91) UUCCUGCCAUAGGAGAUGCCUAAGGCUUU,
 (SEQ ID NO:92) CCCUCAGAUCUGCAUAUAAGCAGCUGC,
 (SEQ ID NO:93) CCCACUGCUUAAGCCUCAAUAAAGCUUGCCUUG, and
 40 (SEQ ID NO:94) UCCCUGUUCGGGCGCCACUGCUAGAGAU.

2. A nucleic acid hybrid formed between an oligonucleotide of claim 1 and a nucleotide polymer sufficiently complementary thereto to allow hybridization under stringent hybridization conditions.

45 3. A probe mix comprising an oligonucleotide of claim 1 and a helper probe.

4. A probe mix as claimed in claim 3, wherein said helper probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 15) TGCGAGAGCGT-CAGTATTAAGCGG, complementary oligonucleotide sequence (SEQ ID NO: 95) CCGCTTAATACTGACGCTCTCGCA, and RNA equivalents thereto (SEQ ID NO: 132) UGCGAGAGCGU-CAGUAUUAAGCGG, and (SEQ ID NO: 136) CCGCUUAUACUGACGCUCUCGCA; or
 50 said helper

probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 16) CTACTTTGGAATATTGCTGGTGATCCTTTCCATCCC, the complementary oligonucleotide sequence (SEQ ID NO: 96) GGGATGGAAAGGATCACCAGCAATATTCCAAAGTAG, and RNA equivalents thereto (SEQ ID NO: 133) CUACUUUGGAAUUAUUGCUGGUGAUCCUUUCCAUCCC, and (SEQ ID NO: 137) GGGAUUGGAAAG-GAUCACCAGCAUAUUAUCCAAAGUAG; or
 55

said helper

probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 17) CCAATCCCCCTTTTCTTTTAAAATTGTGGATG, the complementary oligonucleotide sequence (SEQ ID NO: 97) CATCCACAATTTTAAAAGAAAAGGGGGATTGG and RNA equivalents thereto (SEQ ID NO: 134) CCAUCCCCCUUUUCUUUUAAAAUUGUGGAUG and (SEQ ID NO: 138) CAUCCACAAUUUUAAAAGAAAAGGGGGGAUUGG ; or

said helper

probe is an oligonucleotide having a sequence selected from the group consisting of the oligonucleotide sequence (SEQ ID NO: 18) CTCGCCACTCCCCAGTCCCGCCCA, the complementary oligonucleotide sequence (SEQ ID NO: 98) TGGGCGGGACTGGGGAGTGGCGAG, and RNA equivalents thereto (SEQ ID NO: 135) CUCGCCA-CUCCCCAGUCCCCGCCCA and (SEQ ID NO: 139) UGGGCGGGACUGGGGAGUGGCGAG.

5. An oligonucleotide consisting essentially of a sequence selected from the group of:

SEQ. ID. No. 5: GTCATCCATCCTATTTGTTCTCTGAAGGGTACTAGTAG,

SEQ. ID. No. 10: CTACTATTCTTTCCCCTGCACTGTACCCC,

SEQ. ID. No. 71: GUCAUCCAUCCUAUUUGUCCUGAAGGGUACUAGUAG, and

SEQ. ID. No. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC.

6. The oligonucleotide of claim 5, having a sequence of GTCATCCATCCTATTTGTTCTCTGAAGGGTACTAGTAG (SEQ. ID. NO. 5) or its RNA equivalent GUCAUCCAUCCUAUUUGUCCUGAAGGGUACUAGUAG (SEQ. ID. NO. 71).

7. The oligonucleotide of claim 5, having a sequence of CTACTATTCTTTCCCCTGCACTGTACCCC (SEQ. ID. NO. 10) or its RNA equivalent CUACUAUUCUUUCCCCUGCACUGUACCCC (SEQ. ID. NO. 76).

8. An oligonucleotide consisting essentially of between 10 and 100 nucleotides, sufficiently complementary to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 1: 5'-GACTAGCGGAGGCTAGAAGGAGAGAGATGGG-3' and SEQ. ID. No. 53: 5'-CCCATCTCTCCTTCTAGCCTCCGCTAGTC-3', and the RNA equivalents thereto, SEQ. ID. No. 67: 5'-GACUAGCGGAGGCUAGAAGGAGAGAGAUGGG-3' and SEQ. ID. No. 81: 5'-CCCAUCUCUCUCCUUCUAGCCUCCGCUAGUC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C ; or

sufficiently complementary

to a nucleotide polymer having nucleotide base sequence selected from a group consisting of SEQ. ID. No. 2: 5'-GAAGGCTTTCAGCCCAGAAGTAATACCCATG-3' and SEQ. ID. No. 54: 5'-CATGGGTATTACTTCTGGGCTGAAAGCCTTC-3', and the RNA equivalents thereto, SEQ. ID. No. 68: 5'-GAAGGCUUUCAGCCCCAGAAGUAAUACCCAUG-3' and SEQ. ID. No. 82: 5'-CAUGGGUAAUACUUCUGGGCU-GAAAGCCUUC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C ; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 3: 5'-ATTTGCATGGCTGCTTGATGTCCCCCACT-3' and SEQ. ID. No. 55: 5'-AGTGGGGGGACATCAAGCAGCCATGCAAAT-3', and the RNA equivalents thereto, SEQ. ID. No. 69: 5'-AUUUGCAUGGCUGCUUGAUGUCCCCCACU-3' and SEQ. ID. No. 83: 5'-AGUGGGGGGACAUCAAGCAGCCAUGCAAU-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C ; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 4: 5'-CTTCCCCTTGGTTCTCTCATCTGGCC-3', and SEQ. ID. No. 56: 5'-GGCCAGATGAGAGAACCAAGGGGAAG-3', and the RNA equivalents thereto, SEQ. ID. No. 70: 5'-CUUCCCCUUGGUUCUCUCAUCUGGCC-3' and SEQ. ID. No. 84: 5'-GGCCAGAUGAGAGAACCAAGGGGAAG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C ; or

sufficiently complementary

to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 5: 5'-GTCATCCATCCTATTTGTTCTCTGAAGGGTACTAGTAG-3', and SEQ. ID. No. 57: 5'-CTACTAGTACCCCTCAGGAACAAATAGGATGGATGAC-3', and the RNA equivalents thereto, SEQ. ID. No. 71: 5-

GUCAUCCAUCCUAUUUGUUCUGAAGGGUACUAGUAG-3' and SEQ. ID. No. 85: 5'-CUACUA-GUACCCUUCAGGAACAAUAGGAUGGAUGAC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

5 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 6: 5'-CTCCCTGACATGCTGTCATCATTTCTTCTAGTG-3', and SEQ. ID. No. 58: 5'-CACTAGAA-GAAATGATGACAGCATGTCAGGGAG-3', and the RNA equivalents thereto, SEQ. ID. No. 72: 5'-CUCC-CUGACAUGCUGUCAUCAUUUCUUCUAGUG-3' and SEQ. ID. No. 86: 5'-CACUAGAAGAAUUGAUGA-CAGCAUGUCAGGGAG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

10 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 7: 5'-GTGGAAGCACATTGTACTGATATCTAATCCC-3', and SEQ. ID. No. 59: 5'-GGGATTAGATAT-CAGTACAATGTGCTTCCAC-3', and the RNA equivalents thereto, SEQ. ID. No. 73: 5'-GUGGAAGCA-CAUUGUACUGAUUAUCUAAUCCC-3' and SEQ. ID. No. 87: 5'-GGGAUUAGAUUCAGUACAAUGUG-CUCCAC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

15 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 8: 5'-GCTCCTCTATTTTGTCTATGCTGCCCTATTTCTAA-3', and SEQ. ID. No. 60: 5'-TTAGAAA-TAGGGCAGCATAGAACAAAAATAGAGGAGC-3', and the RNA equivalents thereto, SEQ. ID. No. 74: 5'-GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA-3' and SEQ. ID. No. 88: 5'-UUA-GAAAUAGGGCAGCAUAGAACAAAAUAGAGGAGC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

20 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 9: 5'-CCTTTGTGTGCTGGTACCCATGC-3', and SEQ. ID. No. 61: 5'-GCATGGGTACCAGCACACAAAGG-3', and the RNA equivalents thereto, SEQ. ID. No. 75: 5'-CCUUUGUGUGCUGGUACC-CAUGC-3' and SEQ. ID. No. 89: 5'-GCAUGGGUACCAGCACACAAAGG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

25 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 10: 5'-CTACTATTCTTTCCCCTGCACTGTACCCC-3', and SEQ. ID. No. 62: 5'-GGGGTACAGTG-CAGGGGAAAGAATAGTAG-3', and the RNA equivalents thereto, SEQ. ID. No. 76: 5'-CUACUAUU-CUUUCCCCUGCACUGUACCCC-3' and SEQ. ID. No. 90: 5'-GGGGUACAGUGCAGGGGAAAGAAUA-GUAG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

30 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 11: 5'-AAAGCCTTAGGCATCTCCTATGGCAGGAA-3', and SEQ. ID. No. 63: 5'-TTCCTGCCATAGGA-GATGCCTAAGGCTTT-3', and the RNA equivalents thereto, SEQ. ID. No. 77: 5'-AAAGCCUUAAGGCAU-CUCCUAUGGCAGGAA-3' and SEQ. ID. No. 91: 5'-UCCUGCCAUAAGGAGAUGCCUAAGGCUUU-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

35 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 12: 5'-GCAGCTGCTTATATGCAGGATCTGAGGG-3', and SEQ. ID. No. 64: 5'-CCCTCAGATCCTG-CATATAAGCAGCTGC-3', and the RNA equivalents thereto, SEQ. ID. No. 78: 5'-GCAGCUGCUUAUAUG-CAGGAUCUGAGGG-3' and SEQ. ID. No. 92: 5'-CCCUCAGAUCCUGCAUUAAGCAGCUGC-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

40 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 13: 5'-CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG-3', and SEQ. ID. No. 65: 5'-CCCACTGCT-TAAGCCTCAATAAAGCTTGCCTTG-3', and the RNA equivalents thereto, SEQ. ID. No. 79: 5'-CAAGG-CAAGCUUUAUUGAGGCUUAAGCAGUGGG-3' and SEQ. ID. No. 93: 5'-CCCACUGCUUAAGCCU-CAAUAAAGCUUGCCUUG-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C; or

sufficiently complementary

45 to a nucleotide polymer having a nucleotide base sequence selected from a group consisting of SEQ. ID. No. 14: 5'-ATCTCTAGCAGTGGCGCCCGAACAGGGA-3', and SEQ. ID. No. 66: 5'-TCCCTGTTCCGGGCGCCACTGCTAGAGAT-3', and the RNA equivalents thereto, SEQ. ID. No. 80: 5'-AU-

CUCUAGCAGUGGCGCCCGAACAGGGA-3' and SEQ. ID. No. 94: 5'-UCCCUGUUCGGGCGCCACUG-CUAGAGAU-3', to form a hybrid in 0.05 M lithium succinate buffer containing 0.6 M LiCl at 60°C.

9. An oligonucleotide selected from the group consisting of:

5

(X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),

(X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),

10

(X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),

(X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),

(X) CAGAAGGAGCCACCCCAAGATTTA (SEQ. ID. NO. 23),

(X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),

15

(X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),

(X) AGTGACATAGCAGGAATA (SEQ. ID. NO. 26),

(X) CCATCCTATTTGTTTCCTGAAGGGTAC (SEQ. ID. NO. 27),

20

(X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),

25

30

35

40

45

50

55

(X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),
(X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
(X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
5 (X) GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
(X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),
(X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
10 (X) GCATTAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35),
(X) GCACTGACTAATTTATCTACTTGTTTCATTTCTC (SEQ. ID. NO. 36),
(X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO.
15 37),
(X) TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
(X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
(X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
20 (X) CCCTTCACCTTCCAGAG (SEQ. ID. NO. 41),
(X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
(X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
25 (X) CAAGGGACTTTCGCTGGGGACTTTC (SEQ. ID. NO. 44),
(X) GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45),
(X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
(X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
30 (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
(X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
(X) GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
35 (X) GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51),
(X) CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99),
(X) CUCCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100),
40 (X) GGCAAUGGUACAUCAGGCCAUUACCUAG (SEQ. ID. NO. 101),
(X) GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102),
(X) CAGAAGGAGCCACCCACAAGAUUUA (SEQ. ID. NO. 103),
(X) GACCAUCAUAGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104),
45 (X) CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105),
(X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106),
(X) CCAUCCUAUUUGUCCUGAAGGGUAC (SEQ. ID. NO. 107),
50

- (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108),
 (X) GAAACCUUGUUGAGUCCAAAAUGCGAACCC (SEQ. ID. NO. 109),
 (X) UGUGCCCUUCUUGCCAC (SEQ. ID. NO. 110),
 (X) CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111),
 (X) GUCAUGCACUUGGAAUAUUCUGGUGAUCCUUU (SEQ. ID. NO. 112),
 (X) CAAUACAUGGAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113),
 (X) ACCAAAGGAAUGGAGGUUCUUCUGAUG (SEQ. ID. NO. 114),
 (X) GCAUUAGGAAUCAUUAAGCACAACCAG (SEQ. ID. NO. 115),
 (X) GCACUGACUAAUUUAUCUACUUGUUAUUCUC (SEQ. ID. NO. 116),
 (X) GGGAUUGGAGGAAUGAACAAGUAGAUAAAUAGUCAG (SEQ. ID. NO. 117),
 (X) UGUGUACAAUCUAGUUGCCAUUUCUGGACUACA (SEQ. ID. NO. 118),
 (X) CAAUGGCAGUAUUAUCCACA (SEQ. ID. NO. 119),
 (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120),
 (X) CCCUUCACCUUCCAGAG (SEQ. ID. NO. 121),
 (X) GAGCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122),
 (X) CUUCGUCGCUGUCUCCGCUUC (SEQ. ID. NO. 123),
 (X) CAAGGGACUUUCCGUGGGGACUUUCC (SEQ. ID. NO. 124),
 (X) GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125),
 (X) GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126),
 (X) CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127),
 (X) CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128),
 (X) CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129),
 (X) GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and
 (X) GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131),

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

10. An oligonucleotide selected from the group of oligonucleotides consisting of:

(X) AGTGACATAGCAGGA ACTA (SEQ. ID. NO. 26)

- (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28)
 (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39)
 (X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40)
 (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41)
 (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106)
 (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108)
 (X) CAAUGGCAGUAUUAUCCACA (SEQ. ID. NO. 119)
 (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120) and
 (X) CCCUUCACCUUCCAGAG (SEQ. ID. NO. 121),

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

11. A kit comprising two oligonucleotides selected from the group consisting of:

5

(X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),

(X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),

10

(X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),

(X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),

(X) CAGAAGGAGCCACCCACAAGATTTA (SEQ. ID. NO. 23),

(X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),

15

(X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),

(X) AGTGACATAGCAGGAATA (SEQ. ID. NO. 26),

(X) CCATCCTATTTGTTCTGAAGGGTAC (SEQ. ID. NO. 27),

20

(X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),

(X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),

(X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),

(X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),

25

(X) GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),

(X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),

(X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),

30

(X) GCATTAGGAATCATTCAAGCACAACCAG (SEQ. ID. NO. 35),

(X) GCACTGACTAATTTATCTACTTGTTTCATTTCTC (SEQ. ID. NO. 36),

35

40

45

50

55

(X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37),

5 (X) TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),

(X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),

(X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),

(X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),

10 (X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),

(X) CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),

(X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),

15 (X) GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45),

(X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),

(X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),

20 (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),

(X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),

(X) GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),

(X) GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51),

25 (X) CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99),

(X) CUCCCCCGCUAAUACUGACGCU (SEQ. ID. NO. 100),

(X) GGCAAUUGGUACAUCAGGCCAUUACCUAG (SEQ. ID. NO. 101),

30 (X) GGGGUGGCUCUUCUGAUAAUGCUG (SEQ. ID. NO. 102),

(X) CAGAAGGAGCCACCCCAAGAUUUA (SEQ. ID. NO. 103),

(X) GACCAUCAUAGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104),

(X) CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105),

35 (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106),

(X) CCAUCCUAUUUGUCCUGAAGGGUAC (SEQ. ID. NO. 107),

(X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108),

40 (X) GAAACCUUGUUGAGUCCAAAUGCGAACC (SEQ. ID. NO. 109),

(X) UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110),

(X) CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111),

(X) GUCAUGCUACUUUGGAAUUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112),

45 (X) CAUACAUGGAUGAUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113),

(X) ACCAAAGGAAUGGAGGUUCUUUCUGAUG (SEQ. ID. NO. 114),

(X) GCAUUAGGAAUCAUUAAGCACACCAG (SEQ. ID. NO. 115),

50

55

- (X)GCACUGACUAAUUAUCUACUUGUUAUUCUC (SEQ. ID. NO. 116),
 (X)GGGAUUGGAGGAAAUGAACAAAGUAGAUAAAUAUAGUCAG (SEQ. ID. NO.
 5 117),
 (X)UGUGUACAAUCUAGUUGCCAUAUUCUGGACUACA (SEQ. ID. NO. 118),
 (X)CAAUUGGCAGUAUUAUCCACA (SEQ. ID. NO. 119),
 (X)GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120),
 10 (X)CCCUUCACCUUUCAGAG (SEQ. ID. NO. 121),
 (X)GAGCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122),
 (X)CUUCGUCGCUGUCUCCGCUUC (SEQ. ID. NO. 123),
 15 (X)CAAGGGACUUUCCGUGGGGACUUUC (SEQ. ID. NO. 124),
 (X)GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125),
 (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126),
 20 (X)CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127),
 (X)CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128),
 (X)CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129),
 (X)GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and
 25 (X)GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131),

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

30

12. A kit comprising two oligonucleotides selected from the group consisting of:

- (X)AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26)
 35 (X)AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28)
 (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39)
 (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40)
 40 (X)CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41)
 (X)AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106)
 (X)AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108)
 (X)CAAUUGGCAGUAUUAUCCACA (SEQ. ID. NO. 119)
 45 (X)GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120) and

(X)CCCUUCACCUUUCAGAG (SEQ. ID. NO. 121),

50

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

55

13. A kit comprising oligonucleotides having the following sequences: (X)CTCGACGCAG-
 GACTCGGCTTGCTG (SEQ. ID. NO. 19) or its RNA equivalent (X)CUCGACGCAGGACUCGGCUUG-
 CUG (SEQ. ID. NO. 99), and (X)CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20) or its RNA equiv-
 alent (X)CUCCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100), and SEQ. ID. NO. 1: GACTAGCG-
 GAGGCTAGAAGGAGAGAGATGGG or its RNA equivalent SEQ. ID. NO. 67: GACUAGCGGAGGCUA-
 GAAGGAGAGAGAUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA

polymerase or which enhances initiation or elongation by an RNA polymerase ; or

comprising oligonucleotides having the following sequences: (X)GGCAAATGGTACATCAGGCCA-TATCACCTAG (SEQ. ID. NO. 21) or its RNA equivalent (X)GGCAAUUGGUACAUCAGGCCAUUAUCAC-CUAG (SEQ. ID. NO. 101), and (X)GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22) or its RNA equivalent (X)GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102), and SEQ. ID. NO. 2: GAAGGCTTTCAGCCCAGAAGTAATACCCATG or its RNA equivalent SEQ. ID. NO. 68: GAAGGCUUU-CAGCCCAGAAGUAAUACCCAUG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAGAAGGAGCCACCCCACAA-GATTTA (SEQ. ID. NO. 23) or its RNA equivalent (X)CAGAAGGAGCCACCCCACAAGAUUUA (SEQ. ID. NO. 103), and (X)CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25) or its RNA equivalent (X)CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105), and SEQ. ID. NO. 3: ATTTG-CATGGCTGCTTGATGTCCCCCACT or its RNA equivalent SEQ. ID. NO. 69: AUUUGCAUGGCUG-CUUGAUGUCCCCCACU, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase ; or

comprising oligonucleotides having the following sequences: (X)GACCATCAATGAGGAAGCTG-CAGAATG (SEQ. ID. NO. 24) or its RNA equivalent (X)GACCAUCAUAGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104), and (X)CCATCCTATTTGTTCTGAGGGTAC (SEQ. ID. NO. 27) or its RNA equivalent (X)CCAUCCUAAUUGUCCUGAAGGGUAC (SEQ. ID. NO. 107), and SEQ. ID. NO. 4: CTTCCCCTTGGTTCTCTCATCTGGCC or its RNA equivalent SEQ. ID. NO. 70: CUUCCCCUUGGUUCU-CUCAUCUGGCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA poly-merase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)AGTGACATAGCAGGAAGCTA (SEQ. ID. NO. 26) or its RNA equivalent (X)AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106), and (X)AGATTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28) or its RNA equivalent (X)AGAUUUCUCCUA-CUGGGAUAGGU (SEQ. ID. NO. 108), and SEQ. ID. NO. 5: GTCATCCATCCTATTTGTTCTGAGGG-TACTAGTAG or its RNA equivalent SEQ. ID. NO. 71: GUCAUCCAUCCUAAUUGUCCUGAAGGGUA-CUAGUAG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase ; or

comprising oligonucleotides having the following sequences: (X)GAAACCTTGTTGAGTC-CAAAATGCGAACCC (SEQ. ID. NO. 29) or its RNA equivalent (X)GAAACCUUGUUGAGUCCAAAAUGC-GAACCC (SEQ. ID. NO. 109), and (X)GTGCCCCTTCTTGCCAC (SEQ. ID. NO. 30) or its RNA equivalent (X)UGUGCCCUUCUUGCCAC (SEQ. ID. NO. 110), and SEQ. ID. NO. 6: CTCCCTGACATGCTGTCTAT-CATTTCTTCTAGTG or its RNA equivalent SEQ. ID. NO. 72: CUCCCUGACAUGCUGUCAUUAUUCUU-CUAGUG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase ; or

comprising oligonucleotides having the following sequences: (X)CAGTACTGGATGTGGGT-GATGC (SEQ. ID. NO. 31) or its RNA equivalent (X)CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111), and (X)GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32) or its RNA equivalent (X)GUCAUGCUACUUUGGAUAAUUCUGGUGAUCCUUU (SEQ. ID. NO. 112), and SEQ. ID. NO. 7: GTGGAAGCACATTGTACTGATATCTAATCCC or its RNA equivalent SEQ. ID. NO. 73: GUGGAAGCA-CAUUGUACUGAUUAUCUAAUCCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAATACATGGATGATTTGTATG-TAGGATCTGAC (SEQ. ID. NO. 33) or its RNA equivalent (X)CAUACAUGGAUGAUUUGUAUGUAG-GAUCUGAC (SEQ. ID. NO. 113), and (X)ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34) or its RNA equivalent (X)ACCAAAGGAUUGGAGGUUCUUCUGAUG (SEQ. ID. NO. 114), and SEQ. ID. NO. 8: GCTCCTCTATTTTGTCTATGCTGCCCTATTTCTAA or its RNA equivalent SEQ. ID. NO. 74: GCUCCUCUAAUUUUGUUCUAUGCUGCCCUAAUUCUAA, where X is nothing or comprises a nucleo-tide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GCATTAGGAATCATTCAAGCA-CAACCAG (SEQ. ID. NO. 35) or its RNA equivalent (X)GCAUUAGGAUUAUUAAGCACAACCAG (SEQ. ID. NO. 115), and (X)GCACTGACTAATTTATCTACTTGTTCAATTCCTC (SEQ. ID. NO. 36) or its RNA equivalent (X)GCACUGACUAAUUUAUCUACUUGUUCUUAUUCUC (SEQ. ID. NO. 116), and SEQ. ID. NO. 9: CCTTTGTGTGCTGGTACCCATGC or its RNA equivalent SEQ. ID. NO. 75: CCUUGUGUG-CUGGUACCCAUGC, where X is nothing or comprises a nucleotide sequence recognized by an RNA poly-merase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GGGATTGGAGGAAATGAA-CAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37) or its RNA equivalent (X)GGGAUUGGAGGAAAUGAA-CAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO. 117), and (X)TGTGTACAATCTAGTTGCCATATTCCTG-GACTACA (SEQ. ID. NO. 38) or its RNA equivalent (X)UGUGUACAAUCUAGUUGCCAUAUUCUGGA-CUACA (SEQ. ID. NO. 118), where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39) or its RNA equivalent (X)CAAUUGGCAGUAUUAUCCACA (SEQ. ID. NO. 119), and (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40) or its RNA equivalent (X)GUUUGUAUGUCU-GUUGCUAUUUAU (SEQ. ID. NO. 120), and SEQ. ID. NO. 10: CTACTATTCTTTCCCCTGCACTGTACCCC or its RNA equivalent SEQ. ID. NO. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39) or its RNA equivalent (X)CAAUUGGCAGUAUUAUCCACA (SEQ. ID. NO. 119), and (X)CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41) or its RNA equivalent (X)CCCUUACCCUUUCCAGAG (SEQ. ID. NO. 121), and SEQ. ID. NO. 10: CTACTATTCTTTCCCCTGCACTGTACCCC or its RNA equivalent SEQ. ID. NO. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GAGCCCTGGAAGCATCCAG-GAAGTCAG (SEQ. ID. NO. 42) or its RNA equivalent (X)GAGCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122), and (X)CTTCGTGCTGTCTCCGCTTC (SEQ. ID. NO. 43) or its RNA equivalent (X)CUUCGUCGUCUGUCUCCGCUUC (SEQ. ID. NO. 123), and SEQ. ID. NO. 11: AAAGCCTTAGG-CATCTCCTATGGCAGGAA or its RNA equivalent SEQ. ID. NO. 77: AAAGCCUUAAGGCAUCUCCUAUGG-CAGGAA, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CAAGGGACTTTCCGCTGGG-GACTTTCC (SEQ. ID. NO. 44) or its RNA equivalent (X)CAAGGGACUUUCCGUGGGGACUUUCC (SEQ. ID. NO. 124), and (X)GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45) or its RNA equivalent (X)GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125), and SEQ. ID. NO. 12: GCAGCTGCTTATATGCAGGATCTGAGGG or its RNA equivalent SEQ. ID. NO. 78: GCAGCUG-CUUAUAUGCAGGAUCUGAGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GTACTGGGTCTCTCTGGTTA-GACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), and (X)CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47) or its RNA equivalent (X)CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127), and SEQ. ID. NO. 13: CAAGG-CAAGCTTTATTGAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAG-CUUUAUUGAGGCUUAAGCAGUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GTACTGGGTCTCTCTGGTTA-GACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), and (X)CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48) or its RNA equivalent (X)CU-GAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128), and SEQ. ID. NO. 13: CAAGGCAAGCTTTATT-GAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAGCUUUAUUGAGG-CUUAAGCAGUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)GTACTGGGTCTCTCTGGTTA-GACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126), and (X)GTTCCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50) or its RNA equivalent (X)GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and SEQ. ID. NO. 13: CAAGGCAAGCTT-TATTGAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAGCUUUAUUGAGG-CUUAAGCAGUGGG, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising oligonucleotides having the following sequences: (X)CTCTGGTAAGTACGATCCCT-CA (SEQ. ID. NO. 49) or its RNA equivalent (X)CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129), and (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51) or its RNA equivalent (X)GCAAGCCGA-

GUCCUGCGUCGAGA (SEQ. ID. NO. 131), and SEQ. ID. NO. 14: ATCTCTAGCAGTGGCGCCCGAA-CAGGGA or its RNA equivalent SEQ. ID. NO. 80: AUCUCUAGCAGUGGCGCCCGAACAGGGA, where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

- 5 14. A method for selectively amplifying Human Immunodeficiency Virus type 1 nucleic acid in a sample, comprising the step of amplifying said nucleic acid with one or more oligonucleotides selected from the group consisting of:

10 (X) CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19),
 (X) CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20),
 (X) GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21),
 15 (X) GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22),
 (X) CAGAAGGAGCCACCCACAAGATTTA (SEQ. ID. NO. 23),
 (X) GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24),
 (X) CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25),
 20 (X) AGTGACATAGCAGGAATA (SEQ. ID. NO. 26),
 (X) CCATCCTATTTGTTTCCTGAAGGTAC (SEQ. ID. NO. 27),
 (X) AGATTTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28),
 25 (X) GAAACCTTGTTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29),
 (X) TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30),
 (X) CAGTACTGGATGTGGGTGATGC (SEQ. ID. NO. 31),
 30 (X) GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32),
 (X) CAATACATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33),
 (X) ACCAAAGGAATGGAGGTTCTTTCTGATG (SEQ. ID. NO. 34),
 (X) GCATTAGGAATCATTCAAGCACACCAG (SEQ. ID. NO. 35),
 35 (X) GCACTGACTAATTTATCTACTTGTTCATTTCTC (SEQ. ID. NO. 36),
 (X) GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO.
 37),
 40 (X) TGTGTACAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38),
 (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39),
 (X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40),
 45 (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41),

(X) GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42),
 (X) CTTCTGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43),
 5 (X) CAAGGGACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44),
 (X) GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45),
 (X) GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46),
 (X) CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
 10 (X) CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
 (X) CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49),
 (X) GTTCGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50),
 15 (X) GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51)
 (X) CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99),
 (X) CUCCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100),
 (X) GGCAAUUGGUACAUCAGGCCAUUACCUAG (SEQ. ID. NO. 101),
 20 (X) GGGGUGGCUCCUUCUGAUAAUGCUG (SEQ. ID. NO. 102),
 (X) CAGAAGGAGCCACCCACAAGAUUUA (SEQ. ID. NO. 103),
 (X) GACCAUCAUUGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104),
 25 (X) CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105),
 (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106),
 (X) CCAUCCUAUUUGUUCUGAAGGGUAC (SEQ. ID. NO. 107),
 (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108),
 30 (X) GAAACCUUGUUGAGUCCAAAAUGCGAACCC (SEQ. ID. NO. 109),
 (X) UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110),
 (X) CAGUACUGGAUGUGGGUGAUGC (SEQ. ID. NO. 111),
 35 (X) GUCAUGCUACUUUGGAAUAAUUCUGGUGAUCCUUU (SEQ. ID. NO. 112),
 (X) CAAUACAUGGAUGAUUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113),
 (X) ACCAAAGGAAUGGAGGUUCUUUCUGAUG (SEQ. ID. NO. 114),
 40 (X) GCAUUAGGAAUCAUUAAGCACAACCAG (SEQ. ID. NO. 115),
 (X) GCACUGACUAAUUUAUCUACUUGUUAUUUCCUC (SEQ. ID. NO. 116),
 (X) GGGAUUGGAGGAAAUGAACAAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO.
 117),
 45 (X) UGUGUACAAUCUAGUUGCCAUAUUCUGGACUACA (SEQ. ID. NO. 118),
 (X) CAAUUGGCAGUAUUCAUCCACA (SEQ. ID. NO. 119),
 (X) GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120),
 50

(X) CCCUUCACCUUUCAGAG (SEQ. ID. NO. 121),
 (X) GAGCCCUGGAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122),
 5 (X) CUUCGUCGCGUCUCUCCGCUUC (SEQ. ID. NO. 123),
 (X) CAAGGGACUUUCCGUGGGGACUUUCC (SEQ. ID. NO. 124),
 (X) GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125),
 (X) GUACUGGGUCUCUCUGGUUAGACCA (SEQ. ID. NO. 126),
 10 (X) CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127),
 (X) CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128),
 (X) CUCUGGUAACUAGAGAUCCCUCA (SEQ. ID. NO. 129),
 15 (X) GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130), and
 (X) GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131)

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

15. A method for selectively amplifying Human Immunodeficiency Virus type 1 nucleic acid in a sample, comprising the step of amplifying said nucleic acid with one or more oligonucleotides selected from the group consisting of:

25 (X) AGTGACATAGCAGGAACTA (SEQ. ID. NO. 26)
 (X) AGATTTCTCTACTGGGATAGGT (SEQ. ID. NO. 28)
 (X) CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39)
 30 (X) GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40)
 (X) CCCTTCACCTTTCCAGAG (SEQ. ID. NO. 41)
 (X) AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106)
 35 (X) AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108)
 (X) CAAAUAGGCAGUAUUAUCCACA (SEQ. ID. NO. 119)
 (X) GUUUGUAUGUCUGUUGCUAUUUAU (SEQ. ID. NO. 120) and
 40 (X) CCCUUCACCUUUCAGAG (SEQ. ID. NO. 121),

where (X) is nothing or comprises a nucleotide sequence that is recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase.

- 45 16. A method for detecting Human Immunodeficiency Virus type 1 nucleic acid in a sample comprising the step of hybridizing nucleic acid obtained directly or amplified from said sample with an oligonucleotide selected from the group consisting of:

(SEQ ID NO: 1) GACTAGCGGAGGCTAGAAAGGAGAGAGATGGG,
(SEQ ID NO: 2) GAAGGCTTTCAGCCCAGAAGTAATACCCATG,
5 (SEQ ID NO: 3) ATTTGCATGGCTGCTTGATGTCCCCCCT,
(SEQ ID NO: 4) CTTCCCCTTGGTTCTCTCATCTGGCC,
(SEQ ID NO: 5) GTCATCCATCCTATTTGTTCTGAAGGGTACTAGTAG,
10 (SEQ ID NO: 6) CTCCTGACATGCTGTCATCATTTCTTCTAGTG,
(SEQ ID NO: 7) GTGGAAGCACATTGTACTGATATCTAATCCC,
(SEQ ID NO: 8) GCTCCTCTATTTTTGTTCTATGCTGCCCTATTTCTAA,
(SEQ ID NO: 9) CCTTTGTGTGCTGGTACCCATGC,
15 (SEQ ID NO: 10) CTACTATTCTTTCCCCTGCACTGTACCCC,
(SEQ ID NO: 11) AAAGCCTTAGGCATCTCCTATGGCAGGAA,
(SEQ ID NO: 12) GCAGCTGCTTATATGCAGGATCTGAGGG,
20 (SEQ ID NO: 13) CAAGGCAAGCTTTATTGAGGCTTAAGCAGTGGG,
(SEQ ID NO: 14) ATCTCTAGCAGTGGCGCCCGAACAGGGA,
(SEQ ID NO: 53) CCCATCTCTCTCCTTCTAGCCTCCGCTAGTC,
(SEQ ID NO: 54) CATGGGTATTACTTCTGGGCTGAAAGCCTTC,
25 (SEQ ID NO: 55) AGTGGGGGGACATCAAGCAGCCATGCAAAT,
(SEQ ID NO: 56) GGCCAGATGAGAGAACCAAGGGGAAG,
(SEQ ID NO: 57) CTACTAGTACCCTTCAGGAACAAATAGGATGGATGAC,
30 (SEQ ID NO: 58) CACTAGAAGAAATGATGACAGCATGTGAGGGAG,
(SEQ ID NO: 59) GGGATTAGATATCAGTACAATGTGCTTCCAC,
(SEQ ID NO: 60) TTAGAAATAGGGCAGCATAGAACAAAAATAGAGGAGC,
35 (SEQ ID NO: 61) GCATGGGTACCAGCACACAAAGG,

40

45

50

55

(SEQ ID NO:62) GGGGTACAGTGCAGGGGAAAGAATAGTAG,
 (SEQ ID NO:63) TTCCTGCCATAGGAGATGCCTAAGGCTTT,
 (SEQ ID NO:64) CCCTCAGATCCTGCATATAAGCAGCTGC,
 (SEQ ID NO:65) CCCACTGCTTAAGCCTCAATAAAGCTTGCCTTG,
 (SEQ ID NO:66) TCCCTGTTTCGGGCGCCACTGCTAGAGAT,
 (SEQ ID NO:67) GACUAGCGGAGGCUAGAAGGAGAGAGAUGGG,
 (SEQ ID NO:68) GAAGGCUUUCAGCCCAGAAGUAAUACCCAUG,
 (SEQ ID NO:69) AUUUGCAUGGCUGCUUGAUGUCCCCCACU,
 (SEQ ID NO:70) CUUCCCCUUGGUUCUCUCAUCUGGCC,
 (SEQ ID NO:71) GUCAUCCAUCCUAUUGUUCUGAAGGGUACUAGUAG,
 (SEQ ID NO:72) CUCCCUGACAUGCUGUCAUUAUUCUUCUAGUG,
 (SEQ ID NO:73) GUGGAAGCACAUUGUACUGAUUAUCUAAUCCC,
 (SEQ ID NO:74) GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA,
 (SEQ ID NO:75) CCUUUGUGUGCUGGUACCCAUGC,
 (SEQ ID NO:76) CUACUAUUCUUUCCCCUGCACUGUACCCC,
 (SEQ ID NO:77) AAAGCCUUAGGCAUCUCCUAUGGCAGGAA,
 (SEQ ID NO:78) GCAGCUGCUUAUAUGCAGGAUCUGAGGG,
 (SEQ ID NO:79) CAAGGCAAGCUUUAUUGAGGCUUAAGCAGUGGG,
 (SEQ ID NO:80) AUCUCUAGCAGUGGCGCCCGAACAGGGA,
 (SEQ ID NO:81) CCCAUCUCUCUCCUUCUAGCCUCCGCUAGUC,
 (SEQ ID NO:82) CAUGGGUAUUACUUCUGGGCUGAAAGCCUUC,
 (SEQ ID NO:83) AGUGGGGGGACAUCAAGCAGCCAUGCAAU,
 (SEQ ID NO:84) GGCCAGAUGAGAGAACCAAGGGGAAG,
 (SEQ ID NO:85) CUACUAGUACCCUUCAGGAACAAUAGGAUGGAUGAC,
 (SEQ ID NO:86) CACUAGAAGAAAUGAUGACAGCAUGUCAGGGAG,
 (SEQ ID NO:87) GGGAUUAGAUUAUCAGUACAAUGUGCUUCCAC,
 (SEQ ID NO:88) UUAGAAAUAGGGCAGCAUAGAACAAAAUAGAGGAGC,
 (SEQ ID NO:89) GCAUGGGUACCAGCACACAAAGG,
 (SEQ ID NO:90) GGGGUACAGUGCAGGGGAAAGAAUAGUAG,
 (SEQ ID NO:91) UUCCUGCCAUAGGAGAUGCCUAAGGCUUU,
 (SEQ ID NO:92) CCCUCAGAUCUGCAUUAAGCAGCUGC,
 (SEQ ID NO:93) CCCACUGCUUAAGCCUCAAUAAAGCUUGCCUUG, and
 (SEQ ID NO:94) UCCCUGUUCGGGCGCCACUGCUAGAGAU.

17. A method for detecting Human Immunodeficiency Virus type 1 nucleic acid in a sample comprising the step of hybridizing nucleic acid obtained directly or amplified from said sample with an oligonucleotide selected from the group consisting of:

SEQ. ID. NO. 5: GTCATCCATCCTATTTGTTCTGAAGGGTACTAGTAG,
 SEQ. ID. NO. 10: CTACTATTCTTTCCCTGCACTGTACCCC,
 5 SEQ. ID. NO. 71: GUCAUCCAUCCUAUUUGUCCUGAAGGGUACUAGUAG, and
 SEQ. ID. NO. 76: CUACUAUUCUUUCCCCUGCACUGUACCCC.

18. A method for detecting Human Immunodeficiency Virus type 1 nucleic acid comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CTCGACGCAGGACTCGGCTTGCTG (SEQ. ID. NO. 19) or its RNA equivalent (X)CUCGACGCAGGACUCGGCUUGCUG (SEQ. ID. NO. 99), and (X)CTCCCCCGCTTAATACTGACGCT (SEQ. ID. NO. 20) or its RNA equivalent (X)CUCCCCCGCUUAAUACUGACGCU (SEQ. ID. NO. 100), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 1: GACTAGCGGAGGCTAGAAGGAGAGAGATGGG or its RNA equivalent ID. NO. 67: GACUAGCGGAGGCUAGAAGGAGAGAGAUGGG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GGCAAATGGTACATCAGGCCATATCACCTAG (SEQ. ID. NO. 21) or its RNA equivalent (X)GGCAAUUGGUACAUCAGGCCAUUACCUAG (SEQ. ID. NO. 101), and (X)GGGGTGGCTCCTTCTGATAATGCTG (SEQ. ID. NO. 22) or its RNA equivalent (X)GGGGUUGGCUUCUGAUAAUGCUG (SEQ. ID. NO. 102), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 2: GAAGGCTTTCAGCCCAGAAGTAATACCCATG or its RNA equivalent SEQ. ID. NO. 68: GAAGGCUUUCAGCCCAGAAGUAAUACCCAUG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAGAAGGAGCCACCCACAAGATTTA (SEQ. ID. NO. 23) or its RNA equivalent (X)CAGAAGGAGCCACCCACAAGAUUUA (SEQ. ID. NO. 103), and (X)CCCATTCTGCAGCTTCCTCATTGAT (SEQ. ID. NO. 25) or its RNA equivalent (X)CCCAUUCUGCAGCUUCCUCAUUGAU (SEQ. ID. NO. 105), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 3: ATTTGCATGGCTGCTTGATGTCCCCCACT or its RNA equivalent SEQ. ID. NO. 69: AUUUGCAUGGCUGCUUGAUGUCCCCCACU; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GACCATCAATGAGGAAGCTGCAGAATG (SEQ. ID. NO. 24) or its RNA equivalent (X)GACCAUCAUAGAGGAAGCUGCAGAAUG (SEQ. ID. NO. 104), and (X)CCATCCTATTTGTTCTGAAGGGTAC (SEQ. ID. NO. 27) or its RNA equivalent (X)CCAUCCUAUUUGUCCUGAAGGGUAC (SEQ. ID. NO. 107), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 4: CTTCCCCTTGTTCTCTCATCTGGCC or its RNA equivalent SEQ. ID. NO. 70: CUUCCCCUUGGUUCUCUCAUCUGGCC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)AGTGACATAGCAGGAATA (SEQ. ID. NO. 26) or its RNA equivalent (X)AGUGACAUAGCAGGAACUA (SEQ. ID. NO. 106), and (X)AGATTCTCCTACTGGGATAGGT (SEQ. ID. NO. 28) or its RNA equivalent (X)AGAUUUCUCCUACUGGGAUAGGU (SEQ. ID. NO. 108), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 5: GTCATCCATCCTATTTGTTCTGAAGGGTACTAGTAG or its RNA equivalent SEQ. ID. NO. 71: GUCAUCCAUCCUAUUUGUCCUGAAGGGUACUAGUAG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GAAACCTTGTGAGTCCAAAATGCGAACCC (SEQ. ID. NO. 29) or its RNA equivalent (X)GAAACCUUGUUGAGUCCAAAUGCCAACCC (SEQ. ID. NO. 109), and (X)TGTGCCCTTCTTTGCCAC (SEQ. ID. NO. 30) or its RNA equivalent (X)UGUGCCCUUCUUUGCCAC (SEQ. ID. NO. 110), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 6: CTCCTGACATGCTGTCATCATTTCTTAGTG or its RNA equivalent SEQ. ID. NO. 72: CUCCUGACAUGCUGUCAUCAUUUCUUCUAGUG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAG-TACTGGATGTGGGTGATGC (SEQ. ID. NO. 31) or its RNA equivalent (X)CAGUACUGGAUGUGGGU-GAUGC (SEQ. ID. NO. 111), and (X)GTCATGCTACTTTGGAATATTTCTGGTGATCCTTT (SEQ. ID. NO. 32) or its RNA equivalent (X)GUCAUGCUACUUUGGAUAUUUCUGGUGAUCCUUU (SEQ. ID. NO. 112), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 7: GTGGAAGCACATTGTACTGATATCTAATCCC or its RNA equivalent SEQ. ID. NO. 73: GUG-GAAGCACAUUGUACUGAUUAUCUAAUCCC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAATA-CATGGATGATTTGTATGTAGGATCTGAC (SEQ. ID. NO. 33) or its RNA equivalent (X)CAAUACAUG-GAUGAUUUUGUAUGUAGGAUCUGAC (SEQ. ID. NO. 113), and (X)ACCAAAGGAATG-GAGTTCTTTCTGATG (SEQ. ID. NO. 34) or its RNA equivalent (X)ACCAAAGGAUUGGAGGUUCUUU-CUGAUG (SEQ. ID. NO. 114), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 8: GCTCCTCTATTTTGTCTATGCTGCCCTATTTCTAA or its RNA equivalent SEQ. ID. NO. 74: GCUCCUCUAUUUUUGUUCUAUGCUGCCCUAUUUCUAA; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GCAT-TAGGAATCATTCAAGCACAAACCAG (SEQ. ID. NO. 35) or its RNA equivalent (X)GCAUUAGGAAU-CAUUCAGCACAAACCAG (SEQ. ID. NO. 115), and (X)GCACTGACTAATTTATCTACTTGT-TATTTCTC (SEQ. ID. NO. 36) or its RNA equivalent (X)GCACUGACUAAUUUAUCUACUUGUU-CAUUUCCUC (SEQ. ID. NO. 116), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 9: CCTTTGTGTGCTGGTACCCATGC or its RNA equivalent SEQ. ID. NO. 75: CCUUUGUGUGCUGGUACCCAUGC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAAATGGCAGTATTCATCCACA (SEQ. ID. NO. 39) or its RNA equivalent (X)CAAUUGGCAGUAUU-CAUCCACA (SEQ. ID. NO. 119), and (X)GTTTGTATGTCTGTTGCTATTAT (SEQ. ID. NO. 40) or its RNA equivalent (X)GUUUGUAUGUCUGUUGCUAUUAU (SEQ. ID. NO. 120), or (X)CCCTTCACCTTTCCA-GAG (SEQ. ID. NO. 41) or its RNA equivalent (X)CCCUUCACCUUUCAGAG (SEQ. ID. NO. 121), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 10: CTACTATTCTTTCCCTGCACTGTACCCC or its RNA equivalent SEQ. ID. NO. 76: CUACUAUU-CUUUCCCCUGCACUGUACCCC; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GAGCCCTGGAAGCATCCAGGAAGTCAG (SEQ. ID. NO. 42) or its RNA equivalent (X)GAGCCCUG-GAAGCAUCCAGGAAGUCAG (SEQ. ID. NO. 122), and (X)CTTCGTCGCTGTCTCCGCTTC (SEQ. ID. NO. 43) or its RNA equivalent (X)CUUCGUCGUGUCUCCGCUUC (SEQ. ID. NO. 123), and detecting the amplified nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 11: AAAGCCT-TAGGCATCTCCTATGGCAGGAA or its RNA equivalent SEQ. ID. NO. 77: AAAGCCUUAGGCAUCUC-CUAUGGCAGGAA; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)CAAGG-GACTTTCCGCTGGGGACTTTCC (SEQ. ID. NO. 44) or its RNA equivalent (X)CAAGGGACUUUCCG-CUGGGGACUUUCC (SEQ. ID. NO. 124), and (X)GTCTAACCAGAGAGACCCAGTACAGGC (SEQ. ID. NO. 45) or its RNA equivalent (X)GUCUAACCAGAGAGACCCAGUACAGGC (SEQ. ID. NO. 125), and detecting the amplified nucleic acid with an oligonucleotide comprising the SEQ. ID. NO. 12: GCAGCTGCT-TATATGCAGGATCTGAGGG or its RNA equivalent SEQ. ID. NO. 78: GCAGCUGCUUAUAUGCAGGAU-CUGAGGG; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers (X)GGGATTGGAGGAAATGAACAAGTAGATAAATTAGTCAG (SEQ. ID. NO. 37) or its RNA equivalent (X)GGGAUUGGAGGAAAUGAACAAGUAGAUAAAUUAGUCAG (SEQ. ID. NO. 117), and (X)TGTGTA-CAATCTAGTTGCCATATTCCTGGACTACA (SEQ. ID. NO. 38) or its RNA equivalent (X)UGUGUACAAU-CUAGUUGCCAUAUUCUGGACUACA (SEQ. ID. NO. 118), and detecting the amplified nucleic acid with an oligonucleotide; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

comprising the step of amplifying said nucleic acid with the oligonucleotide polymers

(X)GTACTGGGTCTCTCTGGTTAGACCA (SEQ. ID. NO. 46) or its RNA equivalent (X)GUACUGGGUCU-
CUCUGGUUAGACCA (SEQ. ID. NO. 126), and either

5 (X)CACACAACAGACGGGCACACACTACTTG (SEQ. ID. NO. 47),
(X)CACACAACAGACGGGCACACACUACUUG (SEQ. ID. NO. 127),
(X)CTGAGGGATCTCTAGTTACCAGAGT (SEQ. ID. NO. 48),
(X)CUGAGGGAUCUCUAGUUACCAGAGU (SEQ. ID. NO. 128),
10 (X)GTTCTGGGCGCCACTGCTAGAGAT (SEQ. ID. NO. 50) or
(X)GUUCGGGCGCCACUGCUAGAGAU (SEQ. ID. NO. 130),

15 and detecting the amplified nucleic acid with an oligonucleotide comprising the SEQ. ID. NO. 13: CAAGG-
CAAGCTTTATTGAGGCTTAAGCAGTGGG or its RNA equivalent SEQ. ID. NO. 79: CAAGGCAAG-
CUUUAUUGAGGCUUAAGCAGUGGG; where X is nothing or comprises a nucleotide sequence recog-
nized by an RNA polymerase or which enhances initiation or elongation by an RNA polymerase; or

20 comprising the step of amplifying said nucleic acid with the oligonucleotide polymers
(X)CTCTGGTAACTAGAGATCCCTCA (SEQ. ID. NO. 49) or its RNA equivalent (X)CUCUGGUAACUAGA-
GAUCCCUCA (SEQ. ID. NO. 129), and (X)GCAAGCCGAGTCCTGCGTCGAGA (SEQ. ID. NO. 51) or its
RNA equivalent (X)GCAAGCCGAGUCCUGCGUCGAGA (SEQ. ID. NO. 131), and detecting the amplified
nucleic acid with an oligonucleotide comprising the sequence SEQ. ID. NO. 14: ATCTCTAG-
CAGTGGCGCCCGAACAGGGA or its RNA equivalent SEQ. ID. NO. 80: AUCUCUAGCAGUGGCGCCC-
25 GAACAGGGA; where X is nothing or comprises a nucleotide sequence recognized by an RNA polymerase
or which enhances initiation or elongation by an RNA polymerase.





Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) Publication number : **0 617 132 A3**

(12)

EUROPEAN PATENT APPLICATION

(21) Application number : **94302196.4**

(51) Int. Cl.⁵ : **C12Q 1/70, C12Q 1/68**

(22) Date of filing : **28.03.94**

(30) Priority : **26.03.93 US 40745**

(43) Date of publication of application :
28.09.94 Bulletin 94/39

(84) Designated Contracting States :
AT BE CH DE DK ES FR GB IT LI NL SE

(88) Date of deferred publication of search report :
29.11.95 Bulletin 95/48

(71) Applicant : **GEN-PROBE INCORPORATED**
9880 Campus Point Drive
San Diego California 92121-1514 (US)

(72) Inventor : **McDonough, Sherrol H.**
5005 Maynard Street
San Diego, California 92122 (US)
Inventor : **Ryder, Thomas B.**
1863 Angeles Glen
Escondido, California 92029 (US)
Inventor : **Yang, Yeasing**
13569 Glencliff Way
San Diego, California 92130 (US)

(74) Representative : **Goldin, Douglas Michael**
J.A. KEMP & CO.
14, South Square
Gray's Inn
London WC1R 5LX (GB)

(54) **Probes and method to detect human immunodeficiency virus type 1.**

(57) Amplification oligonucleotides and hybridization assay probes are provided which distinguish Human Immunodeficiency Virus type 1 from other viruses found in human blood tissues.

The probes are nucleotide polymers which hybridize to the nucleic acid region of Human Immunodeficiency Virus type 1 corresponding to bases 763-793 of HIV type 1, (HXB2 isolate GenBank accession number KO3455), or any of the regions corresponding to bases 1271-1301, 1358-1387, 1464-1489, 1501-1540, 1813-1845, 2969-2999, 3125-3161, 4148-4170, 4804-4832, 5950-5978, 9496-9523, 510-542 and 624-651.

EP 0 617 132 A3



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 30 2196

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
D,X	EP-A-0 408 295 (GEN PROBE INC) 16 January 1991 * the whole document *	1,2,5,7, 8,13, 16-18	C12Q1/70 C12Q1/68
X	EP-A-0 525 882 (AKZO NV) 3 February 1993 * the whole document *	1,2,8, 13,16,18	
X	WO-A-91 10746 (CHIRON CORP) 25 July 1991 * the whole document *	1-4, 8-16,18	
X	WO-A-92 01814 (CETUS CORP) 6 February 1992 * the whole document *	1,2,8,9, 11,14, 16,18	
X	EP-A-0 519 338 (HOFFMANN LA ROCHE) 23 December 1992 * the whole document *	1,2,8, 13,16,18	
X	EP-A-0 516 540 (CIS BIO INTERNATIONAL) 2 December 1992 * the whole document *	1,2,5,6, 8,13, 16-18	C12Q
D,X	EP-A-0 403 333 (PASTEUR INSTITUT) 19 December 1990 * the whole document *	1,2,8,9, 13,14, 16,18	
X	WO-A-93 00447 (ABBOTT LAB) 7 January 1993 * the whole document *	1,2,8,9, 11,13, 16,18	
-/--			
The present search report has been drawn up for all claims			
Place of search BERLIN		Date of completion of the search 26 September 1995	Examiner De Kok, A
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

EPO FORM 1501 01.92 (P04C01)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 30 2196

DOCUMENTS CONSIDERED TO BE RELEVANT				
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. CL.5)	
X	WO-A-92 16659 (EASTMAN KODAK COMPANY) 1 October 1992 * page 24, line 24 - line 34 * ---	9-12, 14, 15		
X	EP-A-0 511 712 (EASTMAN KODAK COMPANY) 4 November 1992 * page 9, line 6 - line 20 * ---	9, 14		
X	WO-A-91 08308 (PHARMACIA GENETIC ENGINEERING) 13 June 1991 * page 31; table 1 * ---	9, 14		
X	WO-A-92 00384 (GENSET) 9 January 1992 * the whole document * ---	9, 11, 14		
X	WO-A-93 02215 (ROYAL FREE HOSPITAL SCHOOL OF MEDICINE) 4 February 1993 * the whole document * ---	9, 11, 14		
X	WO-A-92 02638 (CETUS CORPORATION) 20 February 1992 * the whole document * ---	9, 11, 14		TECHNICAL FIELDS SEARCHED (Int. CL.5)
X	WO-A-92 22641 (VIROGENETICS CORPORATION) 23 December 1992 * the whole document * ---	9, 11, 14		
X	EP-A-0 469 610 (SHIONOGI SEIYAKU KABUSHIKI KAISHA) 5 February 1992 * the whole document * ---	9, 11, 14		
P, X	WO-A-93 25707 (INSTITUTO DE SALUD CARLOS III) 23 December 1993 * the whole document * ---	1, 2, 8, 13, 16, 18		
P, X	WO-A-93 07259 (SCLEROSEFORENINGEN) 15 April 1993 * the whole document * ---	1, 2, 8-16, 18		
The present search report has been drawn up for all claims				
Place of search BERLIN		Date of completion of the search 26 September 1995	Examiner De Kok, A	
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application I : document cited for other reasons A : member of the same patent family, corresponding document</p>				

EPO FORM 1503 (01.94) (P04001)



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 30 2196

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
P,X	WO-A-93 13223 (CHIRON CORPORATION) 8 July 1993 * the whole document *	9,11,14	
P,X	WO-A-94 03635 (INSTITUTE OF MOLECULAR BIOLOGY & BIOTECHNOLOGY) 17 February 1994 * the whole document *	9,11,14	
E	EP-A-0 591 914 (BEHRINGWERKE AG) 13 April 1994 * the whole document *	1,2, 8-16,18	
			TECHNICAL FIELDS SEARCHED (Int.Cl.5)
The present search report has been drawn up for all claims			
Place of search BERLIN		Date of completion of the search 26 September 1995	Examiner De Kok, A
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

EPO FORM 1503 03.92 (P04001)



European Patent
Office

EP 94302196

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ All claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for all claims
- ☐ Only part of the claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claims:
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirement of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims 1-8,13 partly,16,17,18 partly: Oligonucleotides for the detection of human immunodeficiency virus type I and their use.
2. Claims 9-12,13 partly,14,15,18 partly: Oligonucleotides for the amplification of human immunodeficiency virus type I and their use.

- ☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respects of which search fees have been paid, namely claims:
- ☐ None of the further search fees has been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

